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ARCHIVES OF OPHTHALMOLOGY

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OCULAR SURGERY

Random Observations

C S O'BRIEN, M D

IOWA CITY

AS AN ocular surgeon and teacher for more than twenty years, one naturally forms certain judgments as to surgical methods and procedures. These are offered herewith in the hope that they may be of benefit to others. Although it is realized that many may be an old story, others may be of interest.

ANESTHESIA

No excuse exists for poor anesthesia. A fearful and uncooperative patient makes for a poor surgical performance.

Preoperative sedation is indicated for all patients. Morphine should not be given before intraocular operations, since it may lead to vomiting. However, its use is quite satisfactory for extraocular surgical procedures.

Cocaine hydrochloride is probably the best of the local anesthetics for instillation. The lids should be kept closed, since cocaine disturbs the corneal epithelium to a less extent under this condition. Also, cocaine should not be instilled for more than ten or twelve minutes; longer periods tend to soften the cornea. Subconjunctival injection of a weak solution of cocaine or procaine enhances deep anesthesia. Since tetracaine hydrochloride, 0.5 per cent, does not act as a mydriatic, it is substituted for cocaine in operations for glaucoma.

A retrobulbar injection of 2 per cent procaine hydrochloride with epinephrine hydrochloride, 1:20,000, results in deep anesthesia of all intraocular structures. This injection should be given into the muscle cone as near the globe as possible in order to reach the ciliary nerves.

AKINESIA

Paralysis of the muscles of lid closure is indicated in any operation in which the globe is to be opened. This is especially true in cataract extraction, in which the incision is large and squeezing may result in loss of vitreous. It is believed that the injection of 2 per cent procaine hydrochloride with epinephrine hydrochloride, 1:20,000, over the condyloid process of the mandible is the procedure of choice.

From the Department of Ophthalmology, State University of Iowa College of Medicine.

Read at a meeting of the New England Ophthalmological Society, Boston, Dec 18, 1945.

PREPARATION FOR INTRAOCULAR OPERATIONS

Epinephrine hydrochloride, 1 1,000, instilled just before an intra-ocular operation induces hemostasis and lessens hemorrhage materially.

It is impossible to sterilize the cornea and conjunctiva, but painting the lid margins, lids and surrounding skin with one-half strength tincture of iodine lessens the chances of infection.

Prior to cataract extraction with peripheral iridotomy or iridectomy the pupil is dilated with homatropine and paredrine hydrobromide ophthalmic.¹

CATARACT EXTRACTION

The injection of typhoid H antigen vaccine intravenously, in a dose of 10,000,000 to 15,000,000 bacilli, two days before operation and repetition, with a dose of 15,000,000 to 20,000,000, on the day prior to operation are routine, and the procedure is believed to lessen post-operative iridocyclitis. Also, in an attempt to reduce infection at operation, penicillin ointment is instilled into the conjunctival sac every two hours for two days.

In modern surgical procedures, it goes without saying that sutures are to be used. Certainly, the corneoscleral type, placed before the incision is made, is desirable. The advantages of such sutures are several: rapid closure of the wound if loss of vitreous is imminent or has occurred, early reformation of the anterior chamber, infrequency of wound separation, rarity of prolapse of the iris, infrequency of post-operative glaucoma, lessening of astigmatism, prevention of corneal eversion and increased activity of the patient during convalescence.

A slightly modified Stallard suture is satisfactory. A knot is made approximately 3 cm. from the end of a 000000 silk suture, which is armed with an atraumatic needle. At 12 o'clock, the suture is passed through the anterior layers of the cornea very close to and parallel with the limbus and then pulled through until the knot rests against the corneal surface. Then directly above and at a distance of about 2 mm. the suture is passed through the conjunctiva and the superficial layers of the sclera in a direction parallel with the corneal suture. This is really just a mattress suture across the limbus. The loops are spread to make way for the incision, iridotomy and delivery of the lens. By pulling on the end of the suture opposite the knot, the wound may be instantly closed at any time.

Simple delicate instruments are always desirable. Use of complicated speculums, locked fixation forceps, and the like, is not advisable since in case of accident one must be able to get out rapidly.

1 Paredrine hydrobromide ophthalmic is a 1 per cent solution of parahydroxy- α -methylphenylethylamine hydrobromide in distilled water, made isotonic with 2 per cent boric acid and preserved with merthiolate 1:50,000.

The keratome-scissors incision is much more easily made and is safer than the full Graefe knife incision. Admittedly, it is not so spectacular and may hurt one's pride a bit but, after all, the patient should receive first consideration. This incision is not such a mental hazard for the beginner or the occasional operator. It is almost impossible to make a poor incision with the keratome and scissors, fixation need not be so secure and if lost may be easily regained, the incision may be made more slowly, aqueous is not lost until the keratome incision is complete, there is no prolapse of iris during the process and, finally, the incision seems to heal more rapidly and firmly. When the incision is completed with scissors, the outside blade is to be laid against the sclera before cutting since thus the incision is back of the limbus and sutures are more easily placed.

In the presence of a very shallow anterior chamber a short Graefe knife incision may be made more easily. Or, better still, a rather long scratch incision is made 1 mm back of and parallel with the limbus and then completed with scissors.

A peripheral iridotomy is desirable, even though delivery of the lens is somewhat more difficult. This handicap is overcome if the assistant exerts counterpressure above during delivery of the lens. Prolapse of the iris is not more common with peripheral iridotomy if corneoscleral sutures are used. The eye has a better appearance, and perhaps the vision is somewhat more acute.

Intracapsular extraction of the lens is advisable. A large bite of capsule is preferable to a small one. During this stage of the operation the speculum should be lifted away from the globe by the assistant, this removes all pressure from the globe and often actually creates suction, as may be seen by the corneal dimpling. When one is delivering the lens through a round pupil, counterpressure exerted just above the upper limbus by the assistant aids in forcing the lens through the opening. Such pressure is released as soon as the lens presents in the wound.

Immediately after extraction of the lens the mattress suture is tied, and four ordinary sutures are placed across the incision, they pass through the tough limbal tissues, on one side, and through episclera and conjunctiva, on the other.

Air injected into the anterior chamber keeps open the angle, thus discouraging formation of synechias, also, it helps to prevent prolapse of the iris during the first three or four days of healing. Care should be exercised to fill only about two thirds of the chamber with air and to keep the air in front of the iris. If air passes through the pupil into the posterior chamber it may cause prolapse of the iris or acute glaucoma by forcing the iris against the chamber angle.

A 1 per cent solution of physostigmine installed after the operation is of assistance in keeping the chamber angle free, in preventing prolapse of the iris and in keeping the air in the anterior chamber

One eye only need have a dressing The patient may be allowed to sit in a chair or lie in bed, as desired

If an extracapsular extraction is made, capsule forceps are preferable to a cystotome The former removes part of the capsule and lens epithelium, consequently, proliferation is lessened and after-cataract is infrequent

AFTER-CATARACT

If the membrane is old and tough, dilaceration with two knife needles may be indicated Or one may make a small keratome incision, introduce a sharp iris hook, pull the membrane out and cut it off

CATARACT AND PRIMARY GLAUCOMA

Opinions differ widely as to the surgical procedure in cases of such a complication Some surgeons prefer to do a preliminary iridectomy, others do a cyclodialysis, but most operators perform an external filtering operation before cataract extraction In my experience, if an external filtering operation is done first and, at a later date, is followed with the usual cataract incision through the bleb, the intraocular pressure often rises as a result of scar formation within the former filtering cicatrix One may, however, make a corneal incision below the bleb, or a lateral incision which does not extend into the filtering area

Other surgeons make a cataract extraction and at the same time perform a complete iridectomy or an iris inclusion If the cataract extraction is performed first, it is difficult to do at a later date an external filtering operation because of the scar

More satisfactory, it seems, is a combined anterior sclerectomy (Lagrange) and cataract extraction An injection of 2 per cent solution of procaine hydrochloride with epinephrine hydrochloride, 1 20,000 is made between Tenon's capsule and the sclera above the upper portion of the limbus Such an injection makes dissection easier and insures a thicker flap The flap is dissected down as usual for the Lagrange operation, and a keratome incision is made well back of the limbus Then, with a Holth punch, a bit of sclera is removed As the next step, a peripheral basal iridectomy is done After this, the incision is enlarged with scissors and the lens is extracted intracapsularly in the usual manner Conjunctival sutures complete the operation

Objection has been made to the combined anterior sclerectomy and cataract extraction because of the slow reformation of the anterior chamber and perhaps the exaggerated formation of anterior synechias In my experience, the anterior chamber reforms almost as rapidly as

after cataract extraction. Often anterior synechias are already present and the angle is closed before operation, otherwise, a filtering operation would not be indicated.

OPERATIONS FOR GLAUCOMA

No operation is always successful in the treatment of glaucoma, even though a complete study of the case is made, the diagnosis is correct and the operation is apparently well done.

Acute Narrow Angle Glaucoma (acute congestive glaucoma) —In the early stages, i. e., within the first two or three days, or if the tension returns to normal with use of miotics, a basal iridectomy is indicated. The incision should not be made with a keratome, for it is almost always anterior to the chamber angle. An incision with a Graefe knife is better, but the anterior chamber is usually emptied too rapidly and the iris tends to prolapse before an iridectomy can be done, this is not especially unsatisfactory if one wishes to do a complete iridectomy. But if a peripheral basal iridectomy is desired the iris must be replaced first, oftentimes a difficult, or even impossible, procedure. The best technic for iridectomy is to enter the anterior chamber through a scratch incision 1.5 mm. back of and parallel with the limbus, the aqueous may be emptied slowly, and a peripheral basal iridectomy is a simple procedure.

Chronic Wide or Narrow Angle Glaucoma (glaucoma simplex) —Cyclodialysis is good practice in cases of chronic wide or narrow angle glaucoma in which the tension is not too greatly elevated, in cases with small visual fields or as a second operation. It is also indicated in cases of postoperative glaucoma following cataract extraction.

Before cyclodialysis is performed, the chamber angle is studied with the gonioscope to determine the position of dense synechias and larger vessels, both of which are to be avoided at operation if possible.

After the conjunctiva is opened, a scleral fixation suture is placed just ahead of the area chosen for the incision. A 0000 twisted silk suture on an atraumatic needle is passed through the anterior layers of the sclera, the two ends are cut short and then grasped close to the sclera with a small hemostat. This gives excellent fixation, in addition, the wound may be made to gape for introduction of the iris repositor.

The iris repositor should be passed through the attachment of the ciliary body with pushing rather than with sweeping movements. One should not go far into the anterior chamber with the spatula, otherwise, the corneal endothelium and Descemet's membrane may suffer undue damage. An absorbent applicator placed at the incision assists in the prevention of hemorrhage into the anterior chamber.

It seems that almost one-half the attachment of the ciliary body should be torn away. Probably the operation has fallen into disrepute because of too little dialysis.

External Filtering Operations—In the Lagrange or Elliott operation, injection of fluid under Tenon's capsule helps to obtain a thick flap. A thick flap, which should include both conjunctiva and Tenon's capsule, protects against late infection through the area of the bleb.

CONVERGENT STRABISMUS

Indications for operation are based on the ocular condition, and not on the age of the patient. It is not wise to perform operation for squint until an attempt has been made to correct it with glasses, to obtain as nearly normal visual acuity as possible, and to develop (1) single binocular vision, (2) normal retinal correspondence and (3) fusion, with some amplitude at the objective angle. It is understood that this cannot always be accomplished—if not, an operation may be performed for cosmetic reasons.

General anesthesia is best for such operations, and pentothal sodium given intravenously can be recommended in operations on children over 5 or 6 years of age.

It seems wise to do a two stage operation in cases of convergent squint for with this method there are few overcorrections. Undercorrection is expected after the first operation. In most cases of convergent squint of over 15 degrees a recession of 5 mm. is made on one internal rectus muscle. After three or more months the lateral rectus is shortened or shortened and advanced, depending on the amount of squint remaining. One never knows the exact amount of recession or resection to make, only great experience is of value, therefore the two stage operation is advisable.

My greatest failures have been with patients who are older and have very poor vision in one eye, those with severe spasm of the inferior oblique, those with abnormal retinal correspondence and, especially, those with eccentric fixation.

In a recession a muscle clamp is never used, since 2 to 3 mm. of muscle is lost. Only a squint hook is used, and the sutures are placed as close to the insertion of the muscle as possible. The muscle sheath is always kept intact.

In cases of resection or of resection and advancement the muscle is attached to the sclera with three sutures. This allows the patient complete use of the eyes soon after operation.

The use of surgical gut U S P (catgut) sutures is advised for both muscle and conjunctiva. Removal of the sutures is then unnecessary. After the operation a thin dressing and an ice cap or ice glove for forty-eight hours reduce the postoperative reaction.

The eyes are allowed to remain open after the ice cap is removed. In cases of advancement in which tension is exerted on the sutures, pin-

hole glasses may be prescribed for a few days in order to reduce ocular movements

TUMORS OF THE ORBIT

After having tried the Kronlein and the brow incision, I have for the past several years used to advantage the following approach to orbital tumors. A wide lateral canthotomy, extending about 1 cm back of the bony orbital margin, is made, and the incision is extended upward or downward in the conjunctival fornix. All tumors except those nasal to the muscle cone may be reached by this incision.

State University of Iowa College of Medicine

MALIGNANT MELANOMA OF LIMBUS AND SPONTANEOUS CYST OF PIGMENTED LAYER OF IRIS IN SAME SECTOR

Contribution to Histogenesis of Tumors

ARNOLD LOEWENSTEIN, M D

GLASGOW, SCOTLAND

AND

JOHN FOSTER, F R C S

LEEDS, ENGLAND

A CASE is reported in which a malignant melanoma of the limbus and a cyst on the posterior surface of the iris occurred in the same sector of the eye

REPORT OF A CASE

A woman aged 33 had always had defective vision in both eyes, and her eyes had been examined annually. The routine test in 1944 had shown no alteration from the previous year, but in 1945 her optician noticed for the first time a dark spot at 9 o'clock on the limbus of the right eye, a month later this was found to have increased rapidly in size. No history could be obtained of injury, inflammation or a mole prior to her last refraction.

Examination—Right Eye With a correction of +3.75 D cyl, axis 180 vision was 6/9. A sausage-shaped, slightly elevated melanotic tumor overlaid and was concentric with the limbus from 8 to 11 o'clock. It was 5 mm long, 2 mm wide and 1 mm thick (fig 1).

Minute tongues of melanotic infiltrations were visible temporally, and pigment spots extended along the small conjunctival and subconjunctival vessels for 1 mm. No such infiltration was visible in the cornea, but small, stellate pigment spots (resembling those composing a congenital pupillary membrane) were scattered in the corneal epithelium 3 or 4 mm around the tumor. The lens was studded with half a dozen small, punctate anterior capsular cataracts, with reduplication. No sign of posterior synechias or of a pupillary membrane was seen with the biomicroscope, and the fundus was normal except for one spot of pigment in the temporal periphery.

Left Eye With a correction of -1.0 D vision was 6/9. This eye also displayed multiple anterior capsular cataracts, with a tendency to reduplication. One of these opacities projected above the surface like an iceberg. Synechias, suggesting old iritis, were present, but no threads of pupillary membrane were seen.

Operation—The tumor was separated from the cornea and episclera with Tooke's knife and scissors in an attempt to remove it with a margin of healthy tissue on all sides. The raw area was covered with a conjunctival flap from the outer side. The eye recovered rapidly and was "white" in a week.

The histologic investigation was performed at the Tennent Institute for Ophthalmology, University of Glasgow (Prof W J B Riddell).

Biopsy of Tumor (fig 2)—The normal squamous epithelium with goblet cells and normal subconjunctival tissue thinned gradually as it approached the edge of the tumor. Even here, however, the basal epithelial cells were pigmented.

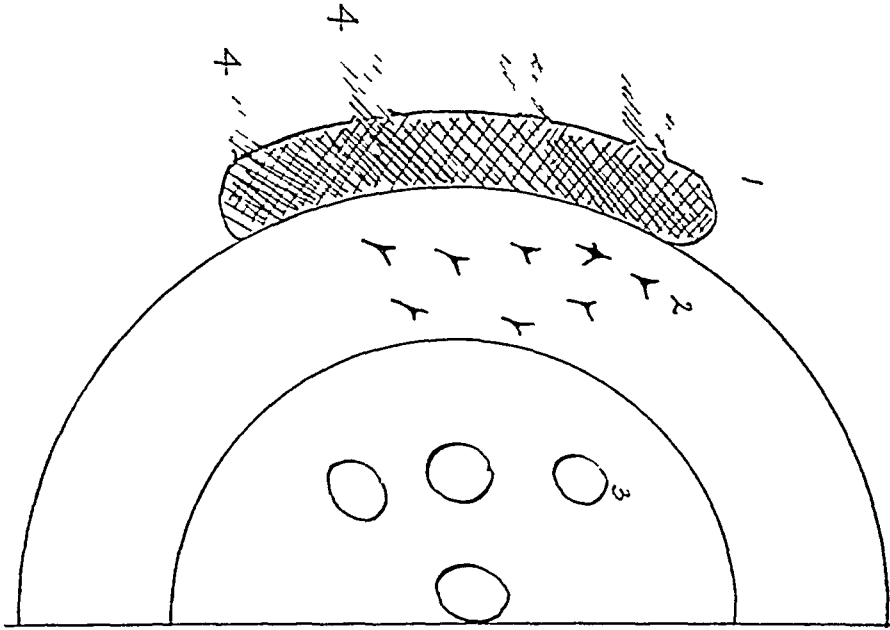


Fig 1—Schematic diagram of limbal melanoma. 1 indicates site of limbal tumor, 2, corneal pigment, 3, punctate cataract, and 4, conjunctival infiltration.

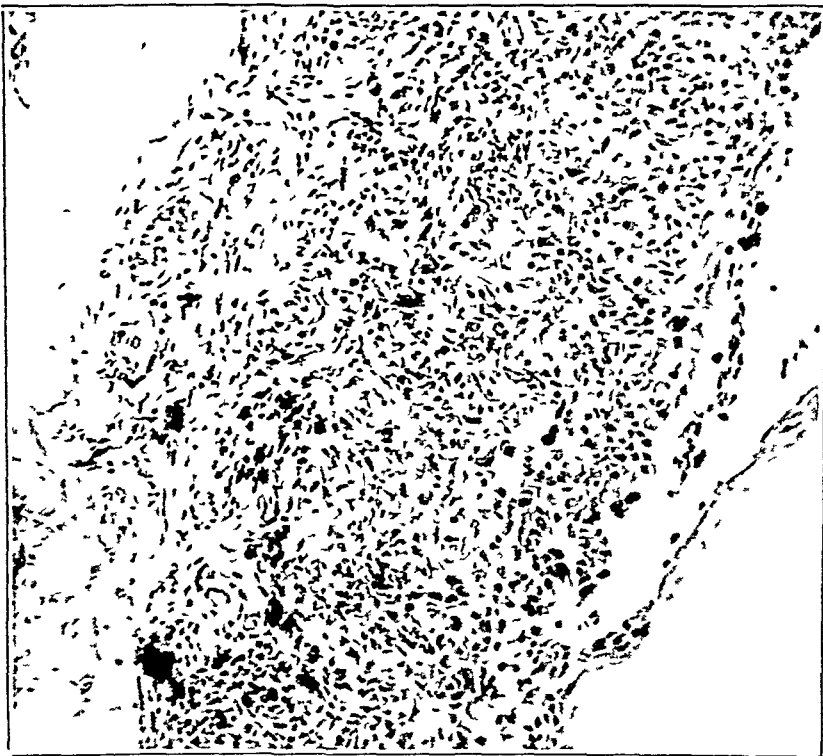


Fig 2—Limbal melanoma, hematoxylin and eosin \times approximately 150.

The intraepithelial islets consisted of cells of varying degrees of pigmentation, located in vacuoles with a loose, unpigmented subepithelial tissue. Even this area showed evidence of malignancy. Around these "cysts," where it overlay the

tumor proper, the epithelium thinned to one or two layers and normal subepithelial connective tissue was absent

The tumor itself consisted of polymorphic nuclei, displaying great variations in shape, size and intensity of staining. Round, polyhedral, spindle-shaped and giant nuclei, five times the average size, were all present. There were few mitoses, and the nucleolus was as a rule indistinct. Coffee brown pigment was largely distributed in all parts of the tumor. Van Gieson's stain revealed little connective tissue, and specific staining showed a low reticulum content. Vascularization was adequate, and necrosis and inflammatory reaction were absent.

While no sharp line of demarcation was present between the tumor and the underlying normal sclera, there was no evidence of infiltration of the deeper layers in the sections we examined.

Enucleation and Examination of Excised Eye—As the tumor cells were of an immature and malignant type, enucleation of the eye was obviously indicated. Care was taken during this operation to excise the conjunctiva widely around the site of the tumor.

Examination with the Slit Lamp After fixation in formaldehyde-saline solution, the back of the globe was removed by a postequatorial section to permit examination with the slit lamp of the entire ciliary body from behind. The view obtained is well shown in figure 3 (painted by Gabriel Donald). The lens was in situ, zonular fibers were traceable, and Hannover's canal was visible. The anterior opacities were not visible through the opaque lens.

No abnormality of the uvea could be detected except for the small, flat, sharply demarcated tumor shown in Donald's picture, which was located at the ciliary side of the iris root and underlay approximately the center of the site of the episcleral tumor. As is also shown in the picture, around this relatively flat tumor were a number of very small, brown, grapelike bodies on the crests and in the valleys of the ciliary processes. No sign of such changes could be found elsewhere with the slit lamp.

Histologic Examination The eye was embedded in pyroxylin, and sections were cut radial to the tumor, every twentieth section being stained and the rest retained for further investigation. The cornea was intact. The episclera at the external site of the tumor was thickened and infiltrated with fibroblasts and lymphocytes (fig. 4). Normal epithelium covered the defect in part. Embedded in the normal tissue of the anterior third of the sclera, and exclusively under the site of the excised tumor, were large pigmented cells. These corresponded in appearance to the dermal (or choroidal) chromatophores, (fig. 5).

Nothing was seen in the sections corresponding to the stellate pigment spots of the cornea except a few clear spots peripherally, where the basal epithelial cells contained a considerable number of vacuoles. It is possible that pigment may have been here, if so, it must have differed from that at the limbus and in the cyst of the iris in being soluble in alcohol. As no tissue was embedded in gelatin for fat staining, we remain uncertain of the nature of the clinically visible corneal pigmentation.

Schlemm's canal beneath the tumor was broad, patent and lined with endothelium (fig. 6). Its posterior wall (on the side of the anterior chamber) consisted of a dense meshwork of six to eight glassy lamellae, whose narrow interstices were filled with chocolate brown pigment. This was of coarser grain than is the pigment usually seen in cases of glaucoma or iritis, and its extension covered the peripheral end of Descemet's membrane (figs. 7 and 8). Nine patent (limbal) vessels could be seen in cross section between Schlemm's canal and the



Fig 3—Slit lamp picture of the cyst and satellites as viewed from behind
The brownish cyst is partly covered by the ciliary processes, $\times 10$

region of the limbus. Five of these were of considerable size. In longitudinal section (fig 7) an empty vessel, probably an aqueous vein of Ascher, could be seen to join the canal.

The deeper layers of the pupillary three fourths of the iris were normal. The pigmented layers of the fourth portion on the ciliary side were split to form a rhomboid cyst, measuring 700 by 400 microns (figs 4 and 6). The cyst was optically empty, and its base was formed by pigmented dilator cells, whose structure was clearly defined. On the pupillary side, the wall of the cyst was thickened and infolded (fig 6). Several loculi were visible in the wall of the cyst on the ciliary side where it was closely attached to the ciliary processes (fig 4). Depigmented sections (fig 9) show the cyst to consist of one row of cubical epithelium, with round nuclei and evenly stained cytoplasm and with no evidence of mucinous changes.

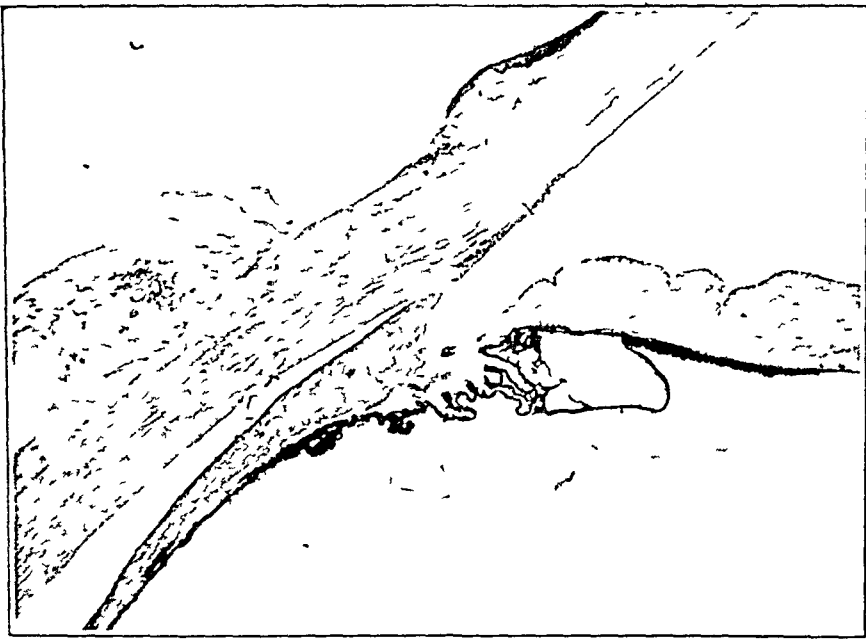


Fig 4—Area of melanoma and spontaneous cyst of pigmentary epithelium of the iris, with several chambers (low power). Note the swollen area of the excised episcleral melanoma.

Several other small cysts (fig 6), lined with one layer of unpigmented epithelium, were observed in the ciliary processes in roughly the same area.

COMMENT

There are two conditions in this eye to be considered—the malignant melanoma of the limbus and the cyst on the posterior surface of the iris. In the absence of operation, disease or injury as a cause in post-natal life, it is probable that the cyst is of congenital origin. As the two lesions are restricted to the same sector of the globe, the chief question concerns their possible causal relationship. Was one lesion in fact caused by the other, or have they a common cause? Previous embryologic and pathologic observations throw some light on this point.

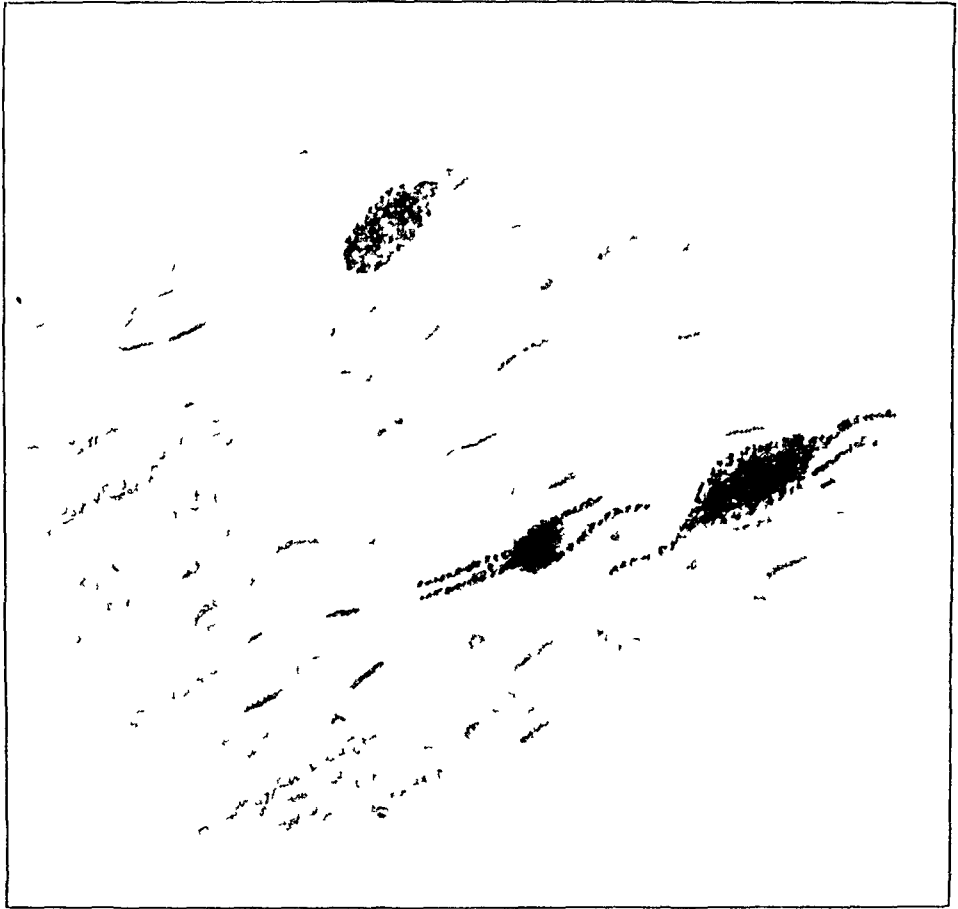


Fig 5—Pigment cells of the stroma in the superficial third of the sclera under the site of the excised melanoma $\times 300$



Fig 6—Spontaneous cyst of the iris. Note the heavily pigmented meshwork behind Schlemm's canal and the cyst in the ciliary body. Hematoxylin and eosin, \times approximately 150

Spontaneous cysts of the pigmented epithelium are alleged to be rare Ginsberg¹ recorded 7 cases only in the world literature up to 1928—a figure which Gilbert repeated in 1930² and Duke-Elder³ increased to 13 in 1940 This does not include the relatively common cysts of ciliary epithelium, which may arise, as indicated by Coats⁴ in 1908, from inflammatory adhesions of the epithelium of contiguous ciliary processes or of the ciliary processes and the iris

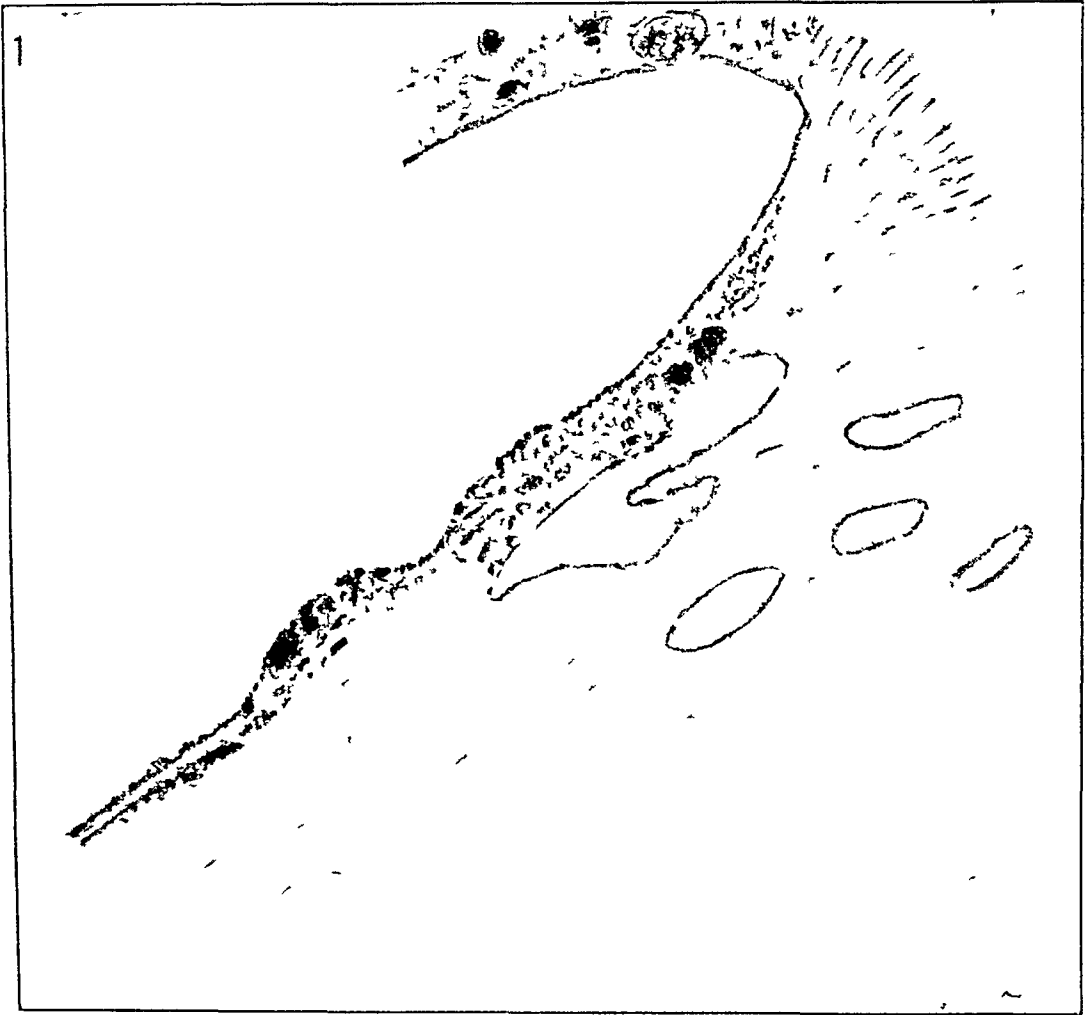


Fig 7—Densely packed coarse pigment behind Schlemm's canal, continued toward and enveloping Descemet's membrane The empty spaces may correspond to aqueous veins of Ascher The spur hints at their confluence with Schlemm's canal Hematoxylin and eosin, $\times 60$

1 Ginsberg, S, in Wessely, K Auge, Berlin, Julius Springer, 1928, vol 1, p 541

2 Gilbert, W, in Schieck, F, and Bruckner, A Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol 5, p 96

3 Duke-Elder, W S Text-Book of Ophthalmology, St Louis, C V Mosby Company, 1940, p 2443

4 Coats, G Roy London Ophth Hosp Rep **17** 143, 1908

Our own observation has confirmed this occurrence on several occasions. The much less frequent spontaneous cysts of the posterior surface of the iris may arise by incomplete obliteration of the gap between the two germinal layers of the secondary optic vesicle. This gap exists, under the name of "von Szily's (ring) marginal sinus," normally as late as the fifth month of fetal life.

Gilbert⁵ (1910) described a solid, noninfiltrating tumor of the iris of epithelial origin, with multilocular cyst formation in its supramarginal

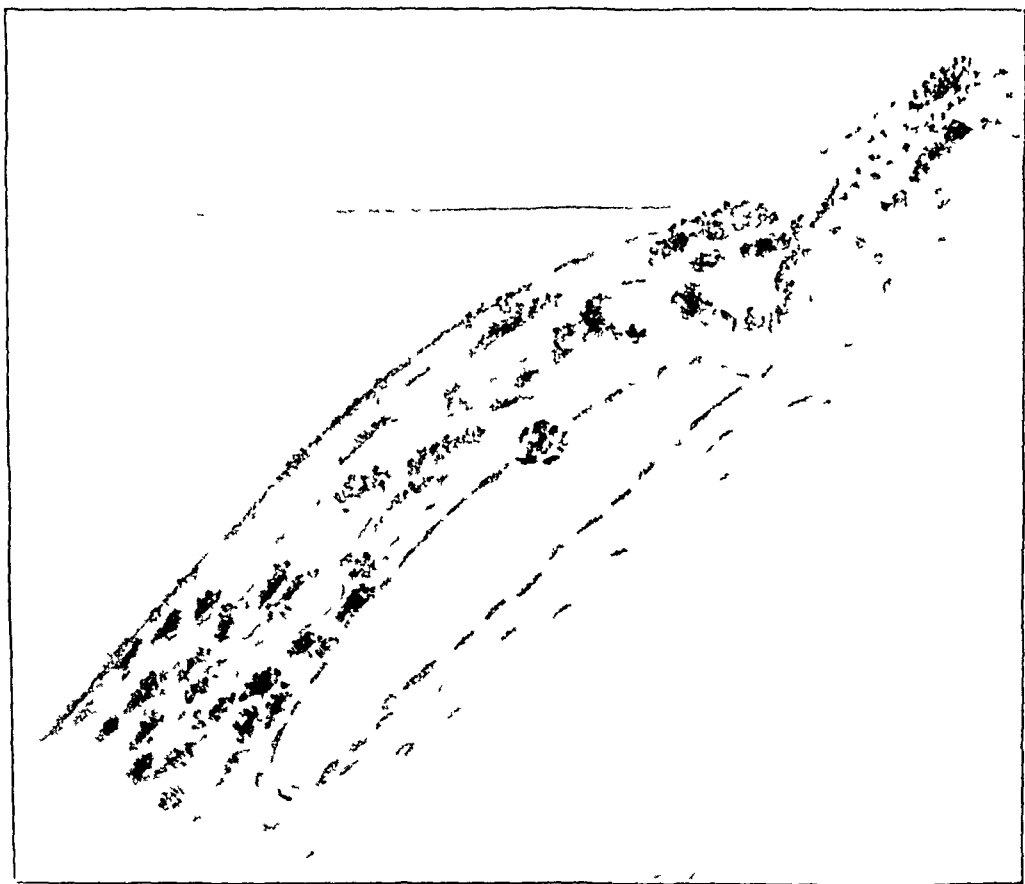


Fig 8—Coarse stroma pigment in front of Schlemm's canal, on the tumor side. There is much less on the opposite side of the section. Hematoxylin and eosin, $\times 300$.

portion. He postulated a primary cyst of the iris arising between two layers of the iris, with the tumor as a secondary, nonmalignant development. It is interesting to note that Tiecher Collins⁶ recorded the occurrence of a small spontaneous cyst between the two pigmented layers of the iris in an eye excised for sarcoma of the ciliary body.

⁵ Gilbert, W. *Klin Monatsbl f Augenh* 48:149, 1910.

⁶ Collins, E. T. *Roy London Ophth Hosp Rep* 13:41, 1890-1891.

Unfortunately, the short description of this case does not include reproductions of the slides

The discovery in our case of a uveal cyst with its satellite patches of brown pigment on the posterior surface of the iris underlying the episcleral melanoma was quite unexpected. This particular area was being examined for evidence of possible melanotic infiltration.

As the slit lamp excluded similar changes elsewhere, one is presented with the coexistence of two relatively rare pathologic conditions in one and the same sector of the eye. Is this a matter of chance only, or is it possible to find a common cause for these two new growths of fundamentally different type? Our ultimate conclusion is that the

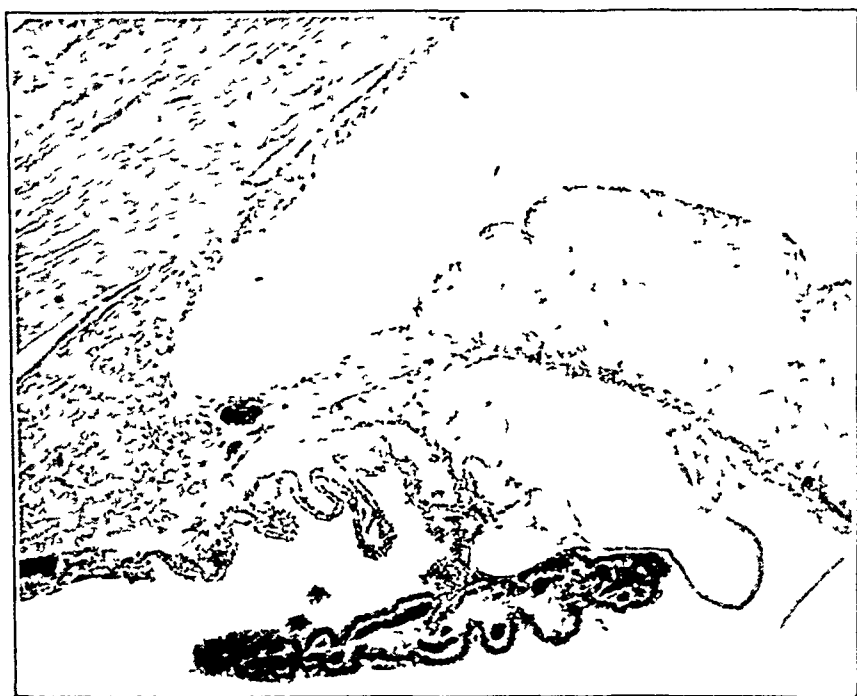


Fig 9—Depigmented epithelium (low power)

internal and external abnormalities we have described were all due to antenatal disturbance, probably inflammatory.

Of course, one cannot be certain at what developmental stage this arose, but it probably antedated formation of the anterior chamber and the complete closure of the cleft between the two germinal layers (16 mm). The changes we have postulated might well occur then. We assume that this process was intrauterine uveitis.

It is common knowledge that the fetal uvea may be affected by septic processes (in the widest sense) in the mother due to a variety of bacteria and viruses. During the past twenty years inexplicable genetic aberrations of a chromosomal character have borne almost the entire blame for congenital abnormalities, and the part played by

fetal inflammation has been greatly underestimated Janků's⁷ observations (1923) regarding that perennial puzzle, coloboma of the macula, met with little support until American authors confirmed his claims by demonstrating that such intrauterine changes could be caused by systemic toxoplasmosis of the mother The embryonic damage due to maternal rubella in the first two months of pregnancy has attracted the attention of the medical world since the publication of Gregg's⁸ paper in 1941 This article is of particular interest to the ophthalmologist in view of the high incidence of congenital cataract associated with these deformities (Long and Danielson⁹)

One might expect that such an inflammatory process could produce the following changes

1 Extension and incomplete obliteration of the space between the two germinal layers leading to cyst formation, the posterior (retinal) layer being detached from the anterior (dilator) layer (as in our case) This explanation has been accepted as the basis of congenital cysts of the posterior part of the iris (Mann¹⁰)

2 Inflammatory dilatation of the vascular element in the tunica vasculosa lentis and intrusion of such vessels into the capsular sac, with disorganization of the developing lens fibers Loewenstein¹¹ (1920) explained the origin of congenital cataract and its association with persistent pupillary membrane in this way, his theory being subsequently confirmed and accepted by Riedel¹² (1922), Pesme¹³ (1927) and others It will be noted that iceberg-like cataracts occurred in both eyes in our case and were associated with posterior synechias in one (the left) eye

3 Simultaneous disturbances in the two layers of the anterior part of the cup about to develop into the pigmented epithelium and the dilator layer of the iris Such potentially pigmented neuroectodermal cells, when displaced as a result of fetal iritis, might give rise to a postnatal melanoma of the limbus

Although the explanation offered of the association observed in our case may be an oversimplification, we do not feel that it is too far fetched It is our hope that application of the technic of examination employed in this case may lead to the discovery of similar cases, which routine histologic technic may easily overlook

7 Janků Časop lek česk **67** 1021, 1923

8 Gregg, N M Tr Ophth Soc Australia **3** 35, 1941

9 Long, J C, and Danielson, R W Cataract and Other Congenital Defects in Infants Following Rubella in the Mother, Arch Ophth **34** 24 (July) 1945

10 Mann, I Developmental Abnormalities of the Eye, London, Cambridge University Press, 1937

11 Loewenstein, A Arch f Ophth **103** 37, 1920

12 Riedel Klin Monatsbl f Augenh **69** 482, 1922

13 Pesme, P Arch d'opt **44** 620, 1927

SUMMARY

A malignant episcleral melanoma, a spontaneous cyst of the posterior tissue of the iris and a heavy deposit of pigment in the meshwork behind Schlemm's canal were observed in the same sector of the eye of a woman aged 33, in addition to a bilateral congenital cataract

It is suggested that fetal inflammation simultaneously produced the cyst, by preventing complete closure of the cleft between the two layers of the optic vesicle, and the melanoma, by displacement of the pigment-storing cells of the outer germinal layer. The congenital cataract and the heavy pigmentation of the meshwork behind Schlemm's canal probably originated in the same inflammatory process

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ATROPHY OF THE OPTIC NERVE FOLLOWING HEMORRHAGE

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AMBLYOPIA following acute loss of blood is an old, but relatively rare, disease. An average of 1 case a year has been reported in the world's literature in the past twenty-five years. Colonel Derrick Vail saw only 4 cases of such visual loss in his vast experience in military ophthalmology in Europe in World War II.

That the pathogenesis of atrophy of the optic nerve following hemorrhage is imperfectly understood is evidenced by the numerous and varied theories (recently summarized by Cox¹) that have been put forth to explain the condition. Knowledge of its pathogenesis is limited because few such blind eyes have ever been examined microscopically. The few histologic studies made have revealed edema of the retinas and optic disks with degenerative changes in the retinal ganglion cells, similar to those associated with quinine poisoning. In addition, Goerlitz² observed foci of degeneration in the optic nerve behind the lamina cribrosa. If conclusions are to be drawn from these microscopic observations, the seat of the disease must lie in the ganglion cells or in their fibers behind the lamina cribrosa, for edema of the optic disk and retina seems insufficient to cause optic nerve atrophy within a few days or weeks. This view is supported by the animal experiments of Holden³ and of Uththoff⁴ and leads to the most tenable explanation of the disease, namely, that retinal ischemia causes degeneration of the ganglion cells, the third retinal neurons, the axons of which constitute the fibers of the optic nerve.

Objections to this theory are the following facts: 1. Hemorrhages of all kinds are frequent, whereas associated visual loss is rare. 2. There is

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1 Cox, R. A. Amblyopia Resulting from Hemorrhage, *Arch Ophth* **32** 368-371 (Nov.) 1944.

2 Goerlitz, M. Blindness Following Severe Loss of Blood. Histologic Study of a Case, *Klin Monatsbl f Augenh* **64** 763-782, 1920.

3 Holden, W. A. The Pathology of the Amblyopia Following Profuse Hemorrhage, *Arch Ophth* **28** 125-134, 1899.

4 Uththoff, W. Blindness and Changes in the Fundus Associated with Anemia, *Ber ü d Versamml d deutsch ophth Gesellsch* **43** 204-212, 1922.

a time lag between the cessation of bleeding and the appearance of blindness, with visual trouble developing between three and sixteen days after the hemorrhage in 39.2 per cent of the cases (Singer⁵). 3 In 15 per cent of the cases the blindness is unilateral. 4 The fundus picture is variable, showing marked papilledema in some cases and no visible retinal changes in other cases. 5 The degree of visual loss does not appear to be dependent on the amount of blood lost, for in some cases this is reported to be small. Furthermore, repeated small hemorrhages are more likely to cause this unfortunate complication than a single large hemorrhage. In view of these objections, it seems plausible that some factor other than ischemia may be playing a role in producing the atrophy of the optic nerve. The process is independent of age, race or sex, and since it rarely, if ever, occurs in a healthy person, Zentmayer⁶ stated the opinion that in all such cases some underlying factor had previously reduced the vitality of the retinal ganglion cells.

Since routine and accurate blood counts and determinations of blood pressure were not practiced before the turn of this century, the 190 cases reported up to 1901 which were exhaustively reviewed by Singer⁵ do not permit an evaluation of the importance of these factors in the causation of the amblyopia following hemorrhage. The 24 cases of Zentmayer⁶ and the 12 cases of Harbridge⁷ represent the literature from 1901 to 1924, but even in this group few blood counts or blood pressure readings were made, and, indeed, many of the patients were not seen by the ophthalmologist until weeks or months after the onset of blindness. The case reports since then are more complete in this respect but leave much to be desired. Inasmuch as the histologic studies of this disease are so meager, clinical and laboratory data must be relied on more heavily in any attempt to shed light on the mechanism of atrophy of the optic nerve. We were able to study a case of partial blindness following severe hemorrhage within twenty-four hours after the patient's complaint of visual loss, and the clinical and laboratory findings are described in some detail.

REPORT OF A CASE

On Dec. 1, 1944, E. W. K., a 34 year old white man, a van driver, was admitted to the Mount Alto Hospital, Washington, D. C., by ambulance for the treatment of a bleeding peptic ulcer. He had been under the care of his private physician for four months, when, on Nov. 27, 1944, he had vomited a large amount of blood and on the following day had fainted. The past history revealed that on induction into the Army, on Oct. 24, 1942, vision was 20/20 in each eye. During his military ser-

⁵ Singer, K. Blindness Following Loss of Blood, *Beitr. z. Augenh.* **53** 1-103, 1904.

⁶ Zentmayer, W. Visual Disturbances from Distant Hemorrhages, *J. A. M. A.* **59** 1050-1055 (Sept. 21) 1912.

⁷ Harbridge, D. F. Optic Atrophy Manifested by Visual Disturbance Following Distant Hemorrhage, *Am. J. Ophth.* **7** 192-196, 1924.

vice, part of which he spent in Africa, he was hospitalized on several occasions because of painful, stiff joints. The hospital records described him at various times as "nervous, apprehensive and slow to answer questions," with a constant coarse tremor of the hands. A history was elicited of alcoholic sprees which lasted a week at a time and had occurred about every two months since the age of 25, although his record was clean in this respect during his military experience. He was discharged from the Army on Aug 11, 1943, with the diagnosis of non-suppurative rheumatoid arthritis. Roentgenograms of the joints, the sedimentation rate and the blood count were repeatedly normal, and the Kahn reaction of the blood was negative.

Examination on admission revealed a tall, pale, confused, dyspneic, restless young man, with a precordial systolic murmur. The systolic blood pressure was 130, and the diastolic pressure was unobtainable. The temperature was 98.4 F^{8a}, the pulse rate, 104, and the respiratory rate, 26. Treatment consisted of sedation, administration of antacids and atropine and giving fluids by mouth. The next day the blood count revealed 1,220,000 red cells with a hemoglobin reading of 25 per cent and 11,000 white cells. The urine was normal, and the Wassermann and Kahn reactions of the blood were negative. A transfusion of 500 cc of citrated blood was given. On the following day the temperature had risen to 103.8 F. On December 4 the patient complained of terrific frontal headache and sudden blindness in the "left side of his left eye." The temperature was 100.8 F, the pulse rate was 124, and the respiratory rate, 26, per minute. The blood pressure was 110 systolic and 0 diastolic. The red blood cell count was 1,550,000, the hemoglobin concentration, 29 per cent, and the white cell count, 6,800.

Ophthalmologic consultation next morning revealed that the pupils were round and equal, reacting well to light and in accommodation. The extraocular movements were good. Determination of the visual fields with the confrontation test revealed temporal hemianopsia in the left eye. The right optic disk was pink, with blurred but not elevated margins. The left disk was enlarged, with blurred edges and a slight elevation of less than 1 D. The nasal half of the disk was definitely pale. In each fundus the arteries were extremely narrowed and the veins widely dilated, with conspicuous arteriovenous nicking. Numerous superficial hemorrhages and some white spots were scattered about bilaterally. The maculae were normal.

The patient continued to complain of severe frontal headache and that night began to vomit "coffee grounds" material and fresh blood clots, falling to the floor in his weakness when he attempted to get out of bed. On December 6 he became disoriented and incontinent of urine. The temperature was 103.2 F, the pulse rate was 140, and the respiratory rate 32, per minute. The blood pressure was 108 systolic and 0 diastolic. The red blood cell count was 900,000, the hemoglobin concentration, 15 per cent, and the white cell count, 11,650. He was given 500 cc of blood in the morning and 500 cc of blood in the afternoon. The next morning he complained of almost complete blindness in the left eye. Examination now revealed marked pallor of the entire left disk, with visual acuity in that eye reduced to the perception of moving shadows at 6 inches (15 cm). Otherwise the fundi were unchanged. Another transfusion of 500 cc of blood was given. On December 8 he was still acutely ill. The temperature was 101 F, the pulse rate was 132, and the respiratory rate 28, per minute. The red cell count was 970,000, the hemoglobin concentration, 15 per cent, and the white cell count, 21,600. Another 500 cc of blood was given. Two days later he complained of some

8a The temperatures listed are the highest for the given day

decrease in the vision of his right eye, but the appearance of the fundus was unchanged. Blood pressure was 120 systolic and 60 diastolic. At night he climbed over the side rails of his bed and tried to leave the hospital. By December 21, all bleeding from the ulcer had ceased, and he had become afebrile. Fluoroscopic examination revealed a duodenal ulcer, and this finding was confirmed by roentgenograms.

Examination on the day of discharge, on Feb 3, 1945, revealed that the pupils were round and equal. They reacted well in accommodation. The right pupil reacted well to light, the left pupil reacted slowly to light through a narrow arc and then dilated rapidly.

Right Eye The optic disk had a hazy superior margin. Its upper half was very pale. The arteries were slightly narrowed, with an artery to vein ratio of 1:2 and with moderate arteriovenous nicking. A patch of white substance lay above the superior temporal vein. The macula was normal. Determination of the visual field revealed a contraction of the temporal half to 50 degrees and a defect in the inferior nasal quadrant. Visual acuity was 20/30 + 2, correctible to 20/15—1.

Left Eye The disk was very pale, with hazy and irregular but not elevated edges. Some of the arteries were narrow, with an artery to vein ratio of 1:3, but the pronounced arteriovenous nicking and dilatation of the veins had disappeared and no white spots or hemorrhages were present. The visual field could not be determined because visual acuity was reduced to light perception but not projection.

The patient was quiet but tremulous, with slow movements and coherent but hesitant speech. The blood count revealed 3,740,000 red cells and a hemoglobin content of 78 per cent.

On examination in the outpatient department three months later, the patient stated that his vision had remained "about the same." The ophthalmologic findings also were essentially unchanged. The pupils were round and equal but dilated, measuring 6 mm. Visual acuity of the right eye was 20/20—2 with ability to read Jaeger type 1, and was correctible to 20/15—1. The disk was flat and somewhat pale, with only the inferior quarter normally pink. The remainder of the fundus was unchanged. The defect in the inferior part of the field was no longer present, so that there was now an almost concentric contraction of the field to five-eighths normal size. The visual acuity and appearance of the fundus of the left eye were unchanged, and the disk was totally white and flat, with rough edges and pronounced narrowing of some of the retinal arteries. The peculiar mental status, with the slow and retarded reaction time and hesitant answers to the simplest questions, was still present. Roentgenograms of the joints showed nothing abnormal. The ophthalmologic findings on reexamination of the patient, on Nov 5, 1945, were identical with those already described.

COMMENT

Analysis of this case reveals sufficient cause for impaired nutrition to the retina. Within a few days after a massive hematemesis the patient had lost four fifths of his red blood cells, causing a reduction in the hemoglobin to 25 per cent, and encroaching seriously on the oxygen-carrying capacity of the blood. Because of continued bleeding this blood picture did not improve for thirteen days, in spite of transfusions totaling 2,500 cc of blood. Failure of the peripheral circulation was present, as evidenced by the weak, rapid pulse and the fact that the diastolic pressure was unobtainable for a week, even though the systolic

pressure was maintained fairly well. Wolff⁸ postulated that this type of amblyopia was due to spasm of the retinal arterioles, resulting from lack of oxygen, while Duggan⁹ attributed it to vasoconstriction produced by an increased output of epinephrine stimulated by the hemorrhage. Whichever one of these mechanisms may have been operating to produce the narrowing of the arteries seen in this patient's fundi, the effect of the decrease in the caliber of the arteries was to increase further the ischemia of the visual elements of the retina. In addition, two days before the patient's visual loss a fever developed, which lasted three weeks. Regardless of its cause (and no focus of infection was ever found), fever causes an increased metabolic rate in all tissues, and thus the need of the retinal cells for oxygen increased at a time when their supply of oxygen was already deficient. In this connection it is interesting to note that Langdon's¹⁰ patient had a rise in temperature to 103 F on the day preceding her visual loss and Long's¹¹ patient had a fever of unknown origin three days before the onset of optic nerve atrophy. The delirium exhibited by the patient for two weeks not uncommonly occurs after severe, acute loss of blood and is generally attributed to cerebral anoxemia. As a result of this mental confusion, the anemia of the brain and the retinal cells was increased, for the patient would not lie flat in bed.

The presence of pallor of part of the optic disk of the right eye a few weeks after the hemorrhage may be attributed to degeneration of the retinal ganglion cells with subsequent gradual ascending atrophy of the optic nerve fibers. The almost concentric contraction of the peripheral field supports this view, for the periphery of the retina has the poorest blood supply. But how is one to explain the atrophy of the medial optic nerve fibers in the left eye occurring suddenly a week after the onset of bleeding and followed two days later by atrophy of the temporal optic nerve fibers? These findings point strongly to direct involvement of the optic nerve fibers in the pathologic process. According to Duke-Elder,¹² the optic nerve fibers at the disk receive their blood supply from recurrent branches of the central retinal artery, supplemented by anastomoses with a few of the short posterior ciliary

8 Wolff, E. The Causation of Amblyopia Following Gastric and Other Hemorrhages, *Tr Ophth Soc U Kingdom* **55** 342-349, 1935

9 Duggan, W. F. Clinical Vascular Physiology of the Eye, *Am J Ophth* **26** 354-368, 1943

10 Langdon, H. M. Amaurosis After Uterine Hemorrhage with Restoration of Vision Following Transfusion, *Arch Ophth* **10** 99-102 (July) 1933

11 Long, A. E. Amaurosis Following Nasal Hemorrhage, *Am J Ophth* **26** 1179-1182, 1943

12 Duke-Elder, W. S. Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1944, pp. 106 and 136

arteries (of the circle of Zinn) These nutrient arteries of the optic nerve are small end arteries, like those of the retina Presumably, if severe hemorrhage can cause a decrease in the quality and quantity of the blood supply to the retina, it can have a similar effect on the blood supply to the optic nerve, with resulting ischemic degeneration of the fibers of the nerve head The observation of Goelitz² of foci of degeneration behind the lamina cribrosa would tend to uphold this view

With this evidence in mind, it would appear that the burden of proof should rest on him who states that ischemia is not the cause of the atrophy of the optic nerve following hemorrhage Moreover, the objections to the theory of retinal ischemia mentioned in the introduction are not applicable in this case While acute hemorrhages of all kinds are frequent, few are so severe that they produce a drop in the hemoglobin to 15 per cent According to the medical literature, only rarely does a human being survive such extreme exsanguination and so acute an anemia—a fact which may account for the rarity of posthemorrhagic atrophy of the optic nerve Also, the disease was bilateral and occurred during, and not after, a prolonged bout of bleeding Nevertheless, like Zentmayer, one cannot but feel that a predisposing factor is present in this malady Terson¹³ emphasized the frequency with which cerebral phenomena accompany posthemorrhagic blindness These he described as coma, violent head pains, polyneuritis, aphasia, amnesia, oculomotor paralyses and deafness Since the metabolism of the brain is identical with that of the inner, or cerebral, part of the retina, it is tempting to attribute the pathologic changes in the two organs to the same factor, namely, ischemia This would furnish a ready explanation for cases like that of Langdon,¹⁰ in which there developed "definite cortical involvement," coincident with atrophy of the optic nerve While my patient, after the clearing of his mental cloudiness, showed none of the neurologic manifestations mentioned by Terson, he did show persistent signs of neuropsychiatric disease, which, as the history revealed, long antedated the duodenal hemorrhage His peculiar mental status presupposes a lack of integrity in the central nervous system, and this element cannot be excluded as a predisposing factor in the causation of the optic nerve atrophy Other examples of the occurrence of this malady in patients with a history of preexistent psychiatric disease are the reports of Harbridge,⁷ who described his patient as "irritable and erratic," and Robertson,¹⁴ whose patient had

13 Terson, A Pathogenesis and Treatment of Visual Disturbances After Loss of Blood, *Ann d'ocul* **159** 23-65, 1922

14 Robertson, C K Sudden Blindness Following Gastro-Intestinal Hemorrhage, *Edinburgh M J* **48** 414-418, 1941

been retired from all work five years previously because of "a marked mental disturbance"

CONCLUSIONS

During a massive hemorrhage from a duodenal ulcer a 34 year old white man experienced partial atrophy of the optic nerve in one eye, with later development in the other eye. Repeated determinations of the blood count and the blood pressure during this illness revealed a persistent state of peripheral circulatory failure and such an extreme acute anemia that ischemia is considered the chief etiologic factor in the production of the pathologic changes observed. The ophthalmologic findings suggest that ischemia can cause atrophy of the optic nerve either by producing degeneration of the retinal ganglion cells or by direct destruction of the optic nerve fibers in the region of the lamina cribrosa. The former mechanism best explains the slow, delayed onset of partial atrophy of the right optic nerve of this patient, whereas the latter mechanism best explains the rapid, early onset of almost total optic atrophy of the left optic nerve.

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TREATMENT OF LEWISITE BURNS OF THE EYE WITH DIMERCAPROL ("BAL")

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EXPOSURE of the eye to relatively small quantities of liquid or vapor lewisite (betachlorovinylchloroarsine) produces a devastating ocular lesion. As will be demonstrated later, the progressive nature of such a burn is caused by the arsenical component of this war gas. To decontaminate the tissues of arsenic after exposure to lewisite, English workers synthesized 2,3-dimercaptopropanol ($\text{CH}_2\text{-SH-CH}_2\text{-SH-CH}_2\text{-OH}$), now called dimercaprol ("BAL"). The work pursued in the laboratories of the Wilmer Ophthalmological Institute was devoted to the determination of the optimum conditions for the use of this antidote, its mode of action and its limitations. These experiments will be discussed under the following headings: (1) the distinctive clinical and pathologic characteristics of lewisite burns of the eye with respect to mode of action, rate of penetration and the time at which irreversible histologic changes first develop, (2) the rate of penetration and persistence of arsenic in the tissues after lewisite burns in relation to the decontaminating action of dimercaprol, and (3) the toxicity and therapeutic efficiency of dimercaprol.

PATHOLOGIC CHARACTERISTICS OF LEWISITE BURNS OF THE EYE

During the course of this work, more than 600 rabbit eyes were exposed to lewisite. The characteristics outlined here were obtained from clinical observations and histologic sections of this material, including burns of all degrees of severity produced by either liquid or vapor lewisite. In general, lewisite burns were characterized by rapid tissue necrosis, pronounced conjunctival and corneal edema and intense exudation. Histologic evidence of corneal damage was found ten minutes after a thirty second exposure to saturated lewisite vapor at 23 C (fig. 1 A). At this time, the basal cells of the corneal epithelium were peglike, somewhat edematous and partially detached from the underlying stroma. The cells of the corneal stroma showed small horizontal clear spaces beneath some of the nuclei, and after thirty minutes the nuclei were

This work was done under a contract, recommended by the Committee on Medical Research, between the Office of Research and Development and the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital.

partially broken up (fig 1*B*) At the end of ten minutes the corneal endothelium was partially disintegrated and serum and fibrin were present in the anterior chamber

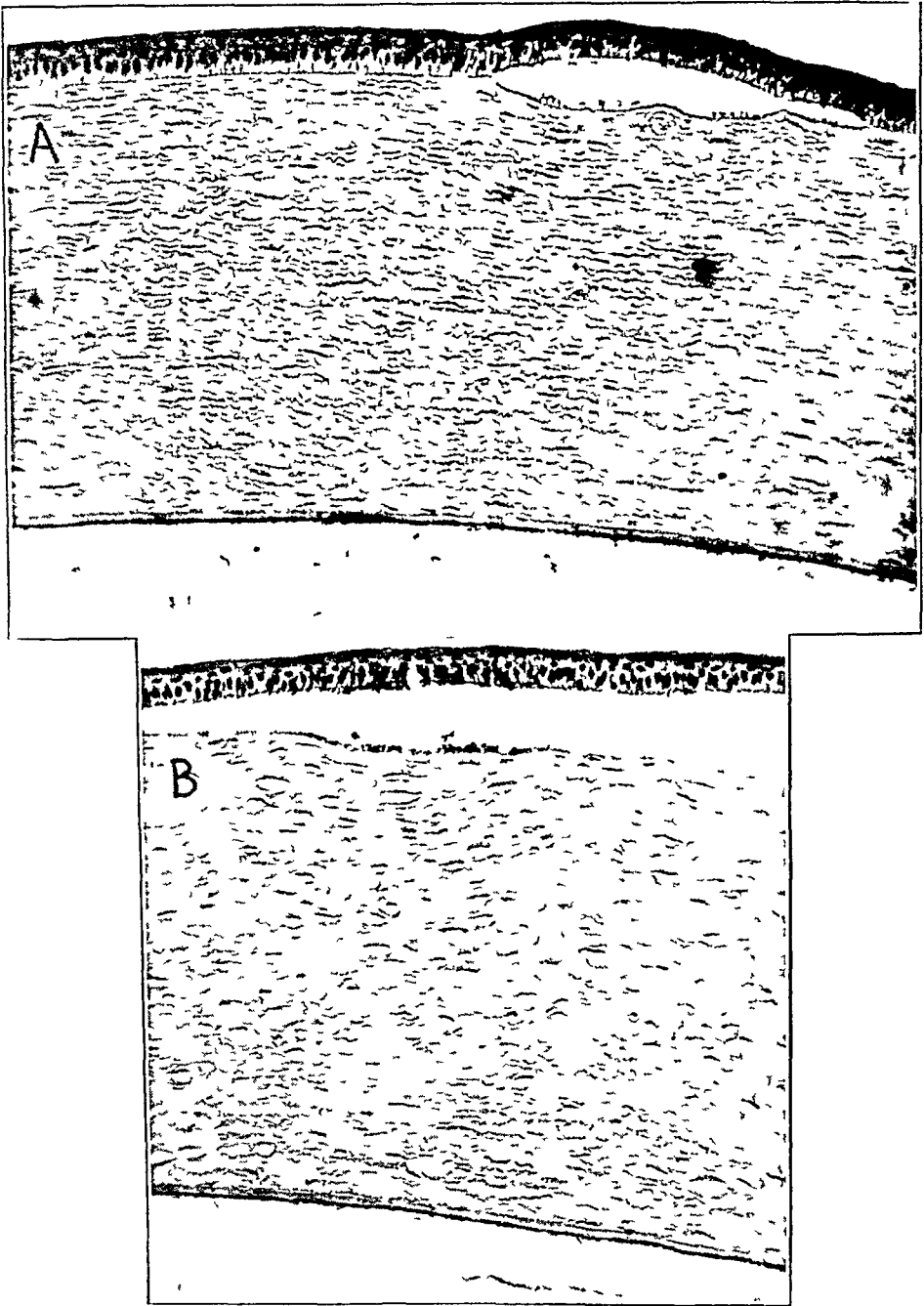


Fig 1—Sections of rabbit cornea (*A*) ten minutes, and (*B*) thirty minutes, after exposure for thirty seconds to saturated lewisite vapor at 22 C

The application of 0.1 mg of liquid lewisite to the surface of the cornea produced instantaneously a dense, circumscribed opacity at the

point of contact. Within five to ten minutes, the localized opacification extended down through one half of the corneal stroma, and small vesicles began to appear on the surface of the involved area. The walls of limbal blood vessels near the site of application were destroyed, producing petechial hemorrhages, thromboses and ischemia (fig 2). Within a few days after the application of liquid lewisite to the limbus, a sector-shaped area of hemorrhage and necrosis of the iris could usually be distinguished directly beneath the site of application. This evidence of deep and localized penetrability of the agent could also be demonstrated histologically.

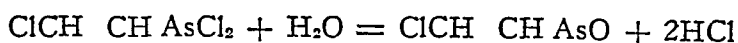
Except for the localized areas of damage produced by the liquid, the subsequent courses of burns produced by vapor and those by liquid lewisite were remarkably similar. Briefly, the changes consisted of



Fig 2—Rabbit eye eleven days after the instillation of 0.1 mg of liquid lewisite on the limbus at 12 o'clock. The small round site of application is still visible, and the surrounding area is ischemic. Corneal vascularization does not proceed from this area.

marked conjunctival edema with petechial hemorrhages and thrombosis of the blood vessels, complete desquamation of the corneal epithelium and edema, purulent infiltration, vascularization and ulceration of the cornea, fibrinous iritis, occasionally secondary glaucoma with staphyloma of the cornea, and cataract.

The Acid Burn Component of Lewisite Burns—The dense superficial area of opacification which appears instantaneously on contact of liquid lewisite with the moist surface of the cornea is probably produced by hydrochloric acid which is liberated by hydrolysis of the lewisite.



Evidence for this view was obtained by the injection of indicator dyes

into beef corneas beneath the sites where lewisite was subsequently applied. It was found that all dyes immediately changed to a color indicative of an acid reaction within a radius of 2 to 4 mm of the site of the lewisite droplet. Thymol blue became red in this area, indicating a local p_H of less than 1.3. Hydrochloric acid solutions of less than p_H 2.5 have been found previously to produce corneal damage.¹

It will be shown later that the use of dimercaprol effectively prevents the progressive development of corneal lesions produced by lewisite. However, the opaque site of application is not altered by such treatment, affording additional evidence that lewisite produces an acid burn, similar to other acid burns, which cause rapid and irreversible precipitation of corneal proteins.¹ Similarly, the superficial corneal haze immediately visible following exposure to lewisite vapor is probably due to the acid portion of hydrolyzed lewisite.

The Arsenical Component of Lewisite Burns—All the later characteristics of a lewisite burn of the eye can be produced by the instillation of a dilute solution of lewisite oxide ($ClCH_2CH_2AsO$). It was found that a number of other compounds containing trivalent arsenic (e. g., sodium meta-arsenite, phenylarsine oxide and oxophenarsine hydrochloride) were more toxic on intracorneal injection of dilute solutions than compounds containing pentavalent arsenic (e. g., sodium arsenate and tryparsamide).

In summary, lewisite hydrolyzes immediately on contact with the moist surface of the eye, producing a superficial acid burn followed by a progressive lesion of the cornea because of the toxicity of the lewisite oxide, which contains trivalent arsenic. Pathologic changes in all tissues of the anterior ocular segment can be detected histologically within ten minutes after exposure, indicating deep penetrability and rapid necrotizing action of this toxic arsenical.

RATE OF PENETRATION AND PERSISTENCE OF ARSENIC IN THE EYES OF RABBITS BURNED WITH LEWISITE

The rate of penetration and the persistence of toxic arsenical material in the cornea and aqueous following exposure to lewisite were determined in order to establish time limits during which either a 100 per cent efficient surface-decontaminating agent or an ideal penetrating agent would be effective.

Materials and Methods—Rabbit corneas were exposed to lewisite, either by the instillation of 0.1 mg. of the liquid onto the center of the cornea or by exposure for thirty seconds at 22 C. to saturated vapor. The lids were closed within thirty seconds after exposure. Then, at varying intervals, the corneas were excised, washed briefly with saline solution and dropped into a solution of arsenic-free

¹ Friedenwald, J. S., Hughes, W. F., Jr., and Herrmann, H. Acid Burns of the Eye, *Arch. Ophth.* **35**: 98 (Feb.) 1946.

nitric acid preparatory to analysis for arsenic by the method of Chaney and Magnuson² With this method, "blank" control tissues may show as much as 0.5 microgram of arsenic. The experimental error for determination of such small amounts of arsenic is about 10 per cent, but any value over 1.0 microgram indicates the definite presence of arsenic. Microchemical estimations of arsenic in the aqueous were also made after the application of 0.1 mg of lewisite to the rabbit cornea near the limbus. Approximately 0.2 cc of aqueous could be obtained by aspiration with a tuberculin syringe and a 26 gage needle. For specimens taken at ten minutes or before, the lids were not closed after the application of

TABLE 1—*Scale for Grading the Severity of Ocular Lesions Produced with Lewisite*

Cornea	Maximum Grade
Density of corneal opacity	8
+ 2 = definite opacity	
+ 4 = blurs iris pattern	
+ 6 = blurs outline of pupil	
+ 8 = completely opaque	
Area of corneal opacity	4
Corneal vascularization (intensity and length)	4
Ulceration	4
+ 1 = staining with fluorescein	
+ 2 = ulceration visible without magnification	
+ 3 = deep slough or marked thinning of cornea	
+ 4 = perforation = 100% corneal lesion regardless of other values	
Edema	4
Total points for estimation of corneal lesion = 24 = 100%	
Duration of corneal opacity	4
+ 1 = 1-3 days	
+ 2 = 4-6 days	
+ 3 = 7-13 days	
+ 4 = 14 days and over	
Conjunctiva	
Redness	2
Edema or chemosis	3
Necrosis (petechial hemorrhages or ischemia)	2
Mucopurulent discharge	2
Iritis	3
+ 1 = small pupil, photophobia or positive aqueous ray	
+ 2 = congestion or thickening of iris	
+ 3 = exudation	

Total Points for Estimation of Ocular Lesion = 40 = 100%

"Maximum ocular reaction" indicates the sum of the maximum values for each symptom during the course of observation and conversion of the total to a percentage figure. This gives an index of the acuteness of the reaction.

"Final corneal opacity" indicates the sum of the values of the corneal symptoms on the last day of observation, a total of 24 points, or corneal perforation representing a 100 per cent lesion. If the cornea became clear, the day on which this occurred is recorded.

lewisite, and the aqueous was withdrawn through a point in the cornea most distant from the site of application. A control analysis indicated that the needle did not become contaminated by any arsenic which might conceivably have spread over the conjunctival or corneal surface.

A second series of experiments was performed to determine the persistence of toxic material on the surface of the cornea, in the cornea or in the aqueous. Direct contact transfers were made from the surface of the exposed eye to the surface of a normal rabbit eye. In order to determine whether the arsenic found within the cornea was still toxic, pressed juice of lewisite-burned corneas was

² Chaney and Magnuson, H. J. *Indust & Engin Chem (Anal Ed)* **12**: 691, 1940.

injected intracorneally into the normal rabbit eyes. The juice of 2 to 4 rabbit corneas previously burned with 0.1 mg. of lewisite was expressed by means of a hydraulic press developing 15,000 pounds of pressure per square inch (1,060 Kg. per square centimeter). Residual cornea tissue consisted only of a dry membrane of tissue paper thinness. The juice was then diluted with 1 cc. of saline solution per cornea and passed through a Seitz bacterial filter. All cultures taken of these filtrates were sterile. One-tenth cubic centimeter of this solution was then

TABLE 2—*Microchemical Analysis of Arsenic in Cornea Following Lewisite Burns of the Rabbit Eye*

Dose of Lewisite	Time After Application	Amount of Arsenic, Micrograms
Controls (no lewisite)		0 — +0.5
0.1 mg. liquid lewisite	2 min.	6.5
		4.1
		6.5
		4.2
		3.7
		2.7
		4.7
	30 min.	1.2
		1.6
	1 hr.	0.7
		2.9
	2 hr.	1.3
	4 hr.	1.8
	11 hr.	0.5
	18 hr.	0.0
	24 hr.	1.7
		0.5
		0.5
	2 days	0.0
	4 days	0.9
Saturated vapor, 22 C. for 30 sec.	2 min.	2.7
		2.9
		3.3
	30 min.	1.2
	1 hr.	1.9
	4 hr.	1.3
	24 hr.	0.8

used for intracorneal injection into normal rabbits. Injection of 0.1 cc. of normal corneal juice does not result in any residual corneal opacification after twenty-four hours. The toxicity of the aqueous at varying intervals after exposure to lewisite was tested by direct intracorneal injection into normal rabbits. The reactions produced by such intracorneal injections were graded according to a numerical evaluation of the symptoms produced, thus giving an index of the toxicity of the material tested (table 1).

Persistence of Toxic Material on the Surface of the Cornea—After the instillation of 0.1 mg. of liquid lewisite on the surface of fresh surviving beef eyes, residual toxic material could still be transferred directly

to rabbit eyes after two and one-half hours. To approximate conditions which would follow a splash burn in a normal human eye, the lids of rabbit eyes were closed within thirty seconds after the instillation of the liquid lewisite, and direct contact transfers to normal rabbit eyes were made at varying intervals thereafter. Transfer after one minute resulted in a 10 per cent reaction in the recipient eye, with clearing of the cornea in three days. Transfer after two to four minutes produced only minor transient conjunctival symptoms, without corneal damage. No toxic material could be transferred after four minutes had elapsed.

Two minutes after exposure to lewisite vapor, no reduction in arsenic content was produced by washing the corneal specimens with saline solution, indicating that free lewisite no longer remained on the surface of the cornea after this interval.

Persistence of Arsenic and Toxic Material in the Cornea—Two minutes after the instillation of 0.1 mg. of lewisite, about 4.6 micro-

TABLE 3—*Toxicity of Corneal Juice After Instillation of 0.1 Mg. of Liquid Lewisite into a Rabbit Eye*

Time After Instillation of Lewisite	Maximum Ocular Reaction Produced by Intracorneal Injection of Corneal Juice into Normal Rabbit Eye
2 min	47
30 min	30
1 hr	17
26 hr	2
27 hr	2
4 days	2 (two injections)

grams of arsenic was demonstrated within the corneal substance (table 2). In terms of lewisite, this is equivalent to about 10 per cent of the original dose applied. This amount of arsenic fell rapidly within the next thirty minutes to 1.4 micrograms, and after eleven hours only traces of arsenic were detected, and then irregularly. About 3 micrograms of arsenic was found within the cornea two minutes after the standard vapor burn was produced. The arsenic content was greatly diminished or absent after twenty-four hours.

Corneal juice obtained two minutes after production of the standard liquid burn caused a 47 per cent maximum ocular reaction when approximately one tenth of the juice was injected into a normal cornea (table 3). This toxicity progressively decreased in the course of thirty minutes and one hour and was absent at the end of twenty-six hours.

Rate of Penetration and Persistence of Arsenic and Toxic Material in the Aqueous—Arsenic penetrated into the anterior chamber within one and one-half minutes after the application of 0.1 mg. of lewisite to the cornea and disappeared within thirty minutes after the exposure

(table 4) The aqueous was found to be toxic at the end of two minutes and ten minutes but had become nontoxic when tested at the end of thirty minutes (table 5)

Surface Decontamination After Exposure to Liquid Lewisite—In view of the foregoing evidence that lewisite rapidly disappears from the surface of the cornea and penetrates into the cornea and aqueous, little or no therapeutic effect would be expected from the use of neutralizing agents which do not penetrate into the ocular tissues This was found

TABLE 4—*Microchemical Analysis of Arsenic in Aqueous Following Instillation of 0.1 Mg of Lewisite on the Rabbit Cornea*

Time After Instillation of Lewisite	Amount of Arsenic, Micrograms
Aqueous control (no lewisite)	0.4 (blank of method = 0.0 to 0.5 microgram)
Needle control (for surface contamination in withdrawing aqueous)	0.2
1 min	0.5
1.5 min	2.2
5 min	2.8
10 min	3.2 (2 specimens)
20 min	3.2
30 min	0.0
1 hr	0.0
2 hr	0.5
11 hr	0.9

TABLE 5—*Toxicity of Aqueous After Instillation of 0.1 Mg of Liquid Lewisite into a Rabbit Eye*

Time After Instillation of Lewisite	Maximum Ocular Reaction Produced by Intracorneal Injection of Aqueous into Normal Rabbit Eye
2 min	47
5 min	45
10 min	32
30 min	0
1 hr	0
24 hr	0
27 hr	0
4 days	0

to be the case with three types of agents tried (1) saline solution used in irrigation, (2) an iodine-containing solution, so-called Box I,³ which inactivates lewisite in fifteen seconds in vitro, and (3) hydrogen peroxide (table 6)

3 This solution was devised by Dr Leslie Hellerman as a method for the continuous regeneration of a limited low concentration of iodine

Sodium iodide	200 mg /100 cc
Phosphate buffer p_H 7	M/10
Sodium iodoxybenzoate in large excess	
Solvent	50% triacetin, 22% alcohol, 28% water

TREATMENT OF LEWISITE BURNS OF THE EYE WITH DIMERCAPROL

Since lewisite penetrates through the cornea into the aqueous within two minutes after exposure and produces irreversible changes in the tissues of the anterior ocular segment soon after ten minutes have elapsed, a successful decontaminating agent must have the capacity to penetrate rapidly and to compete successfully for both free and combined arsenic within the tissues. To obtain the maximum therapeutic effect from the local use of dimercaprol after exposure to lewisite, the following variables were studied: (1) local toxicity of dimercaprol for both the normal and the lewisite-burned eye, (2) optimum concentrations of dimercaprol and technics of application to the eye, (3) time limits during which treatment is efficacious and (4) species differences in toxicity and therapeutic effectiveness of dimercaprol.

Materials and Methods—Both liquid and vapor burns were produced in the eyes of mongrel rabbits and liquid burns in the eyes of *Macacus rhesus* monkeys.⁴

TABLE 6—*Surface Decontamination of the Rabbit Eye Two Minutes After Instillation of 0.1 Mg. of Lewisite*

Number of Eyes	Decontaminating Agent	Maximum Ocular Reaction (%)	Final Corneal Opacity (%)	Days
3	100 cc saline solution in irrigation	72% (S D = 10)*	75% (S D = 19)	7
3	"Box I"—iodine solution ⁵	66% (S D = 3)	69% (S D = 2)	7
6	2% hydrogen peroxide (3 drops)	69% (S D = 4)	65% (S D = 6)	7
3	Blood catalase alternating with 5% hydrogen peroxide every 5 sec for 1 min	63% (S D = 20)	50% (S D = 30)	7
42	No treatment	74% (S D = 8)	69% (S D = 14)	7

* S D = standard deviation of the mean

with lewisite containing 95 per cent of the active substance ($\text{ClCH}_2\text{CHAsCl}_2$). The liquid lewisite was loaded directly into a 0.25 cc Luer tuberculin syringe. Because lewisite appeared to tarnish the stainless steel needles, a 26 gage platinum-iridium needle with a blunt point and gold-plated hilt was used, and care was taken to prevent moisture from precipitating the arsine oxide within the tip of the needle. The syringe was fitted with a micrometer in which one unit turn drove the plunger of the syringe down $\frac{1}{200}$ inch (0.1 mm), displacing a volume of 0.1 cu mm. Droplets of this size were then put in contact with the cornea. Estimations of arsenic immediately following such an instillation on 10 rabbit corneas revealed that only 0.09 mg, or 0.05 cu mm, of lewisite was actually delivered from the needle to the cornea—in other words, only 50 per cent of the theoretic quantity.

Rabbit eyes were exposed to saturated lewisite vapor at controlled temperatures by inserting the individual eye, proptosed between the lids, into the mouth of the Scholz vapor chamber.⁵ All experiments were carried out with the animals

4 These experiments were performed on monkeys, which were made available to me by Dr. Cornelius P. Rhoads, Memorial Hospital, New York.

5 Scholz, R. O. Personal communication to the author.

under ether anesthesia. The eyelids were closed within thirty seconds after exposure of the proptosed eye to either liquid or vapor lewisite.

The severity of the lesion produced was evaluated numerically by grading the important clinical symptoms elicited by the toxic agent (table 1). In order to obtain single values which could be used for statistical comparisons, the acuteness of the reaction was estimated by adding the maximum values for each symptom over the course of observation and converting the total to a percentage figure, the "maximum ocular reaction." An index of persistent corneal damage was obtained by adding the values of the corneal symptoms on the last day of observation, a total of 24 points or corneal perforation representing a 100 per cent lesion.

Preliminary experiments were devoted to the production of a reproducible and uniform standard lesion with lewisite, the technic and dosage to be used in treatment experiments. In general, it is necessary that the lesion be sufficiently severe to guarantee reproducibility, and yet an excessive dose should be avoided, which might mask the efficacy of a therapeutic agent of low potency. Such a threshold

TABLE 7—*Severity of Lesions in Rabbit Eyes Following Standardized Exposure to Lewisite*

Type of Exposure	Number of Eyes	Maximum Ocular Reaction (%)	Final Corneal Opacity (%)	Number of Days Followed
0.1 mg. liquid lewisite	42	74 (S D = 8)*	69 (S D = 14)	7
	37	87 (S D = 8)	85 (S D = 19)	14
Exposed for 30 sec. to saturated vapor at 21-25 C	18	70 (S D = 7)	63 (S D = 14)	7
	18	84 (S D = 10)	82 (S D = 14)	14

* S D = standard deviation of the mean

lesion was produced by the instillation of 0.1 mg. of liquid lewisite either on the limbus or on the center of the cornea, usually resulting in perforation of the cornea within two weeks. A somewhat less severe, but consistent, lesion was produced by exposure of the eye to saturated lewisite vapor at 22 to 24 C for thirty seconds. For use in treatment experiments, it was found that the optimum period of observation was seven days, since increased variability of the standard lesions was noted during the second week, probably as the result of secondary infection. The average values obtained for the standard lesions are given in table 7, together with the standard deviation of the mean.

Preliminary treatment experiments were made with a sample of dimercaprol ("BAL") obtained in the spring of 1942 from Dr. Peters' laboratory at Oxford. Little difference in toxicity or therapeutic efficacy could be made out between the British and the American sample. The American sample appeared to be slightly more toxic at higher concentrations and more therapeutic at lower concentrations, but the British sample was older at the time of comparison. Subsequent experience with later samples of American dimercaprol has shown results comparable to those reported here for the earlier sample.

Suitable solvents for dimercaprol were found in propylene glycol, ethylene glycol, redistilled thiodiethanol and triacetin. The substance is sparingly soluble and deteriorates rapidly in water but is effective therapeutically in aqueous solution. Because of many practical advantages in applying ointments to the eye, an oint-

ment containing dimercaprol was devised and prepared by Mr. Robert S. Fuqua, chief pharmacist of the Johns Hopkins Hospital, for use in these experiments

	Percentage
Dimercaprol	5.10
Benzyl benzoate	5
Peanut oil	20
Absorbent base	20
Cetyl alcohol	10
Glycerin monostearate	14
Liquid petrolatum	21

This ointment was readily miscible with the tears of the eye and became semi-fluid within a minute after instillation. It was nontoxic for the normal rabbit and monkey eye and showed therapeutic efficacy comparable to that of dimercaprol in glycol solution.

Local Toxicity of Dimercaprol—The tolerance of the normal cornea to dimercaprol was determined for rabbit and monkey eyes and partially for human eyes (table 8). The instillation of 0.1 cc. of a 50 or 35 per cent solution of dimercaprol in propylene glycol produced severe

TABLE 8—*Tolerance of the Normal Eye to 0.1 Cc. of Various Solutions of Dimercaprol ("BAL")*

Species	Concentration of Dimercaprol, per Cent	Solvent	Maximum Ocular Reaction	Final Corneal Opacity	Days
Rabbit	50	Propylene glycol	67	67	7
	35	Propylene glycol	40	13	7
	25	Propylene glycol	20	0	2
	15	Propylene glycol	20	0	1
	10	Propylene glycol	5	0	0
	10	Ointment	2	0	0
	5	Propylene glycol	5	0	0
	3	Propylene glycol	5	0	0
	3	Water	2	0	0
Monkey	50	Propylene glycol	42	38	7
	35	Propylene glycol	37	21	6
	25	Propylene glycol	22	0	4
	15	Propylene glycol	0	0	0
	10	Propylene glycol	2	0	0
	10	Ointment	0	0	0
	5	Propylene glycol	0	0	0
Human—2 eyes 3 eyes	10	Propylene glycol	7	0	0
	5	Propylene glycol	5	0	0

corneal damage in both rabbits and monkeys. This was characterized by a sheetlike opacification of the superficial layers of the cornea, which, if not unduly severe, sloughed off within a few days leaving clear stroma beneath. A 25 per cent solution of dimercaprol produced rather pronounced conjunctival reactions without corneal damage, and a 15 per cent solution produced a similar conjunctival reaction in rabbits but none in monkeys. A 10 per cent concentration or less caused no significant objective damage to the eye of the rabbit, monkey or man. The 10 per cent ointment and the 3 per cent aqueous solution of dimercaprol were nontoxic.

Since the development of an ocular lesion is almost completely prevented by the use of 2 drops of a 5 per cent solution of dimercaprol within two minutes after exposure to lewisite (see next section), the more severe reactions which follow the use of higher concentrations must be attributed to the toxic action of the therapeutic agent. This damage produced by dimercaprol can be distinguished clinically in an eye previously burned with lewisite. It is noteworthy that the reactions

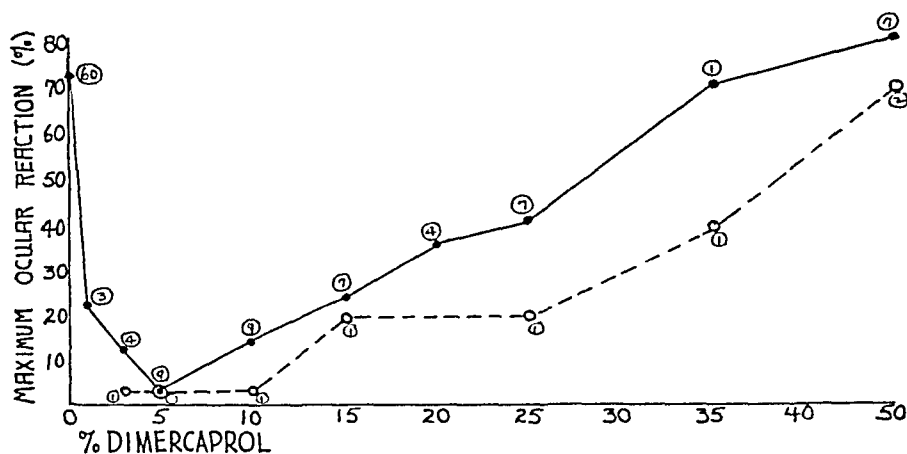


Fig 3—Effect of variations in the concentration of dimercaprol ("BAL") on reactions in normal rabbit eyes and in rabbit eyes burned with lewisite

Values for eyes burned with either vapor or liquid lewisite and treated with 2 drops of a 5 per cent solution of dimercaprol in propylene glycol are indicated by the solid line and dots, values for normal eyes similarly treated, by the broken line and hollow circles. The numerals indicate the number of eyes tested.

TABLE 9—Effect of Variation in Concentration of Dimercaprol ("BAL") in Treatment of Lewisite Burns of the Rabbit Eye *

Concentration of Dimercaprol Solution, per Cent	Number of Eyes	Maximum Ocular Reaction, per Cent	Final Corneal Opacity, per Cent	Number of Days of Follow Up Observation
25	1	45	0	6
20	3	37	0	6
15	4	23	0	4
10	3	11	0	2
5	5	4	0	1
3	2	12	0	2
1	1	20	0	2
Untreated †	42	74 (S D = 8) ‡	69 (S D = 14)	7

* Instillation of 2 drops of dimercaprol in propylene glycol two minutes after application of 0.1 mg of liquid lewisite

† Instillation of 2 drops of propylene glycol had no influence on the severity of the lewisite lesion

‡ S D = standard deviation of the mean

produced by concentrations of dimercaprol of over 5 per cent in eyes previously exposed to lewisite are more severe than those produced by dimercaprol on the normal cornea (fig 3). This suggests that lewisite lowers the tolerance of the cornea for dimercaprol.

Optimum Concentrations of Dimercaprol and Technics of Application in the Treatment of Lewisite Burns—In the first of these experiments, standard burns produced with 0.1 mg of liquid lewisite were treated two minutes later with 0.1 cc of varying concentrations of dimercaprol in propylene glycol (table 9). Although all these concentrations, from 25 to 1 per cent, prevented the development of any corneal opacity lasting more than eight days, the use of 5 per cent solution also



Fig 4—*A* and *B*, eyes exposed for thirty seconds to saturated lewisite vapor at a temperature of 22 C twenty-four hours previously. The right eye (*B*) was treated two minutes after exposure with 0.1 cc of a 5 per cent solution of dimercaprol ("BAL") in propylene glycol, and the left eye (*A*) was not treated. *C* and *D*, eyes exposed in a manner similar to that of the eyes shown in *A* and *B* four days previously and treated similarly.

prevented the development of any significant conjunctival reaction. Similar results were obtained in the treatment of vapor burns. There is, therefore, a moderately wide range of concentrations which produce spectacular cures of lewisite burns (fig 4 *A* and *B*).

Experiments were carried out to determine the effect of larger doses or repeated instillations of various concentrations of dimercaprol. One instillation of 2 drops of solutions of 10 per cent concentration and over produced more reaction than the use of a single drop. The optimum time for the instillation of a second drop was after sixty minutes. Instillation of 1 drop of a 10 per cent solution of the British preparation every ten seconds for one minute, or every fifteen seconds for three minutes, produced severe corneal damage.

Two drops (0.1 cc.) of a 5 per cent solution of dimercaprol will theoretically neutralize about eighty times the standard dose of 0.1 mg. of liquid lewisite used in these experiments. However, the results of treatment following the instillation of 10 mg. of liquid lewisite were not nearly as good, probably because of the large area of instantaneous opacification produced by the acid component of the large lewisite droplet. The instillation of 2 drops of 10, 5 and 1 per cent solutions of dimercaprol two minutes after the instillation of 10 mg. of lewisite resulted in corneal opacities at the end of seven days of 67, 46 and 100 per cent, respectively. Similar treatment with 5 per cent dimercaprol of an eye exposed four times as long as that required for the standard vapor burn (i. e., two minutes) gave a maximum ocular reaction of 42 per cent and a final corneal opacity of 4 per cent at the end of seven days.

The use of 5 per cent dimercaprol ointment was found to be at least as effective as glycol solutions of the substance in the treatment of both liquid and vapor lewisite burns.

Time Limits During Which Dimercaprol Is Effective—The instillation of dimercaprol in solution or ointment form within two minutes after the end of exposure to lewisite usually prevented the development of any significant conjunctival or corneal reaction. If treatment was delayed for five minutes, a transitory conjunctival and corneal reaction ensued, lasting a few days. Treatment ten minutes after exposure was definitely less effective, a mild to moderate corneal opacity persisting at the end of seven days. The use of dimercaprol within the first half-hour lessened the severity of the ocular lesion as compared with control eyes, but the damage to the eye was permanent.

These findings are in agreement with the observation that irreversible histologic changes are already detectable in the corneal stroma within ten minutes after exposure to lewisite and are fairly pronounced after thirty minutes. Also, at the end of thirty minutes, much of the arsenic has already disappeared from the tissues, and so the benefit derived from decontamination is diminished.

Use of Dimercaprol in Other Species—Eleven eyes of monkeys were burned with liquid lewisite and 8 were treated with dimercaprol (table 10). The therapeutic efficacy and optimum concentrations of dimer-

caprol for monkeys were not significantly different from those found in the treatment of rabbit eyes

Two drops of a 5 or 10 per cent solution of dimercaprol in propylene glycol was instilled into the eyes of 6 patients,⁶ and 2 drops of propylene glycol alone was instilled into the eye of a seventh subject. Four patients had noninflamed blind eyes, 1 had low grade uveitis, 1 had a tuberculoma of the ciliary body which had eroded through the sclera, producing intense congestion externally, and 1 had bullous keratitis and glaucoma secondary to irradiation. In summary, it was found that the instillation of 0.1 cc. of a 5 or 10 per cent solution of dimercaprol in propylene glycol produced an immediate stinging sensation, at least partially due to the propylene glycol. In eyes not previously congested, blepharospasm prevented voluntary opening of the lids for about two minutes. The stinging sensation disappeared within five to thirty minutes. Pronounced lachrimation followed the instillation of the

TABLE 10—*Treatment with Dimercaprol of Monkey Eyes Burned with 0.1 Mg. of Liquid Lewisite*

Dimercaprol Concentration, per Cent	Maximum Ocular Reaction, per Cent	Final Corneal Opacity, per Cent	Number of Days of Follow Up Observation	Comment
15	32	29	6	0.1 cc. dimercaprol in propylene glycol applied 2 min. after exposure unless otherwise noted
10	5	0	2	Average for 3 eyes
10	0	0	1	Dimercaprol ointment used
5	8	0	3	Average for 2 eyes
3	10	0	3	
0	57	55	7	Average for 3 eyes

solution within a few seconds and disappeared in twenty to thirty minutes. Congestion of the conjunctival vessels with moderate edema of the conjunctiva developed within a minute or two and persisted for several hours. No evidence of damage to the normal cornea was detected by slit lamp examination and staining with fluorescein. In 2 eyes previously congested as a result of glaucoma and uveitis, respectively, severe and protracted ocular pain followed the instillation of solution of dimercaprol. A temporary exacerbation of the bullous keratitis occurred in 1 case. One patient with chronic noncongestive glaucoma and a second patient with glaucoma secondary to irradiation showed a reduction in intraocular tension of 12 mm. of mercury (Schiotz tonometer) following the instillation of the drug. No subjective differences could be detected between the effect of the 5 and that of the 10 per cent solution.

⁶ These patients include 1 tested by Dr. Jonas S. Friedenwald and a second reported on by Dr. Cornelius P. Rhoads and Dr. Algernon S. Reese.

PERSISTENCE OF ARSENIC IN THE CORNEA AFTER THE
APPLICATION OF DIMERCAPROL

The quantity of arsenic remaining in the cornea at stated intervals after a standard exposure to lewisite vapor was determined both for eyes treated with dimercaprol and for untreated controls (table 11). Whereas a trace of arsenic was demonstrated in the untreated corneas

TABLE 11—*Influence of Dimercaprol on Rate of Disappearance of Arsenic from the Rabbit Cornea After Lewisite Vapor Burns*

Specimen Number	Dimercaprol	Time of Eversion of Cornea	Amount of Arsenic, Micrograms
1	0	2 min	27
2			29
3			33
4		30 min	12
5		1 hr	19
6		1 hr	13
7		24 hr	08
8	2 drops of 5 per cent dimercaprol solution	30 min	00
9		4 hr	00
10		24 hr	00

after twenty-four hours, the corneas treated with 5 per cent dimercaprol showed no residual arsenic after thirty minutes. Thus, the use of dimercaprol facilitates the disappearance of arsenic from the tissues, probably by competing favorably with arsenic reversibly bound to the tissue components.

TABLE 12—*Intravenous Treatment of Lewisite Burns of the Rabbit Eye with 15 per Cent Dimercaprol in Propylene Glycol*

Rabbit Number	Eyes	Weight of Rabbit, Kg	Dose of Dimercaprol, Cc	Time of Treatment, Min	Maximum Ocular Reaction, per Cent	Final Corneal Opacity, per Cent	Days	Comment
1		2.03	1.2	3			1	Rabbit died with convulsion
2	Right	1.8	0.5	2	37	0	7	Mild convulsions
	Left				47	25	7	
3	Right	2.0	0.4	15	47	6	7	Rabbit jittery
	Left			30	57	58	7	

INTRAVENOUS TREATMENT OF LEWISITE BURNS OF THE EYE
WITH DIMERCAPROL

Toxic doses of English "BAL" (dimercaprol) were administered intravenously to 2 rabbits into whose eyes 0.1 mg of lewisite had previously been instilled (table 12). The conjunctival, and to some extent the corneal, reaction in these 2 animals was less than the average ocular reaction in control animals.

SUMMARY AND CONCLUSIONS

Exposure of the eye to small quantities of lewisite liquid or vapor can produce a progressive lesion of the cornea, characterized by rapid tissue necrosis, pronounced edema and intense exudation. Lewisite is immediately hydrolyzed at the site of contact with the moist surface of the eye, liberating hydrochloric acid sufficient to produce a superficial corneal opacity. The more destructive characteristics of lewisite burns can be produced by a neutral solution of lewisite oxide containing the trivalent arsenic. Within two to four minutes after exposure to lewisite followed by closure of the lids, all toxic arsenical material disappears from the surface of the cornea, and within two minutes the drug can be demonstrated in the aqueous. Beginning ten minutes after exposure and becoming well marked in thirty minutes, irreversible histologic changes in the cornea can be detected.

A single instillation of 5 per cent dimercaprol solution or ointment from within two to five minutes after exposure to lewisite effectively prevents the development of serious ocular lesions. This excellent therapeutic effect of dimercaprol is due, in part at least, to its rapid penetration and withdrawal of toxic arsenical material from the tissues before irreversible histologic changes have developed.

OCULAR CHANGES IN THE BLOOD DYSCRASIAS

I S TASSMAN, M D
PHILADELPHIA

IN CONSIDERING a group of diseases in which certain lesions in the eyes may develop, it is necessary to refer to features and conditions peculiar to these diseases which may influence to some extent the signs and symptoms that are likely to occur

The blood dyscrasias include a very large group of disorders, with a variety of etiologic factors and with certain clinical manifestations. Moreover, there appears to exist a close relationship among many of these diseases, with only certain differences in their causation, which may determine the character of the blood picture, the clinical manifestations and the changes which may occur in the eyes. This is especially true of that part of the group designated as "the anemias."

For the purpose of simplicity, the more important diseases of the blood are here grouped according to the changes which occur in the individual constituents of the blood.

Diseases of Blood	Erythrocytes and Hemoglobin	Leukocytes	Platelets
1 Excess of red cells Polycythemia, erythrocytosis	Increased, color index low	Increased	Increased
2 Anemias			
Pernicious anemia	Decreased, color index high	Commonly decreased	Greatly diminished
Secondary	Decreased, color index low	Slightly increased	
Anemia of pregnancy	Increase in blood volume	Slightly increased	
Chlorosis	Decreased, color index low	Usually decreased	Unaffected or increased
3 Leukemias	Decreased	Increased, with number of abnormal cells	Decreased, with variable increase in chronic myelogenous form
4 Purpura hemorrhagica	Decreased	Slightly increased	Greatly decreased

EXCESS OF RED CELLS

Polycythemia—This condition has been described by Whitby and Britton¹ as an excess of cells in the blood. They classified the disease as primary and secondary polycythemia, the primary form being known as erythremia and the secondary form as erythrocytosis. In the primary form, there are an "unexplained hyperplasia of the erythron with polycythemia, an increased blood volume and often an increase in the number of capillary blood vessels." In the secondary form, there are hyper-

Presented at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Nov 19, 1945

1 Whitby, L. E. H., and Britton, C. J. C. Disorders of the Blood, ed 4, Philadelphia, The Blakiston Company, 1942

tiophy of the erythron and polycythemia as a compensatory reaction. The blood is thereby given an increased oxygen-carrying capacity in cases in which tissue oxygenation is imperfectly performed by a normal blood.

Cohen,² in a review of the lesions of the fundus complicating polycythemia, with a report of cases, pointed out that while the general manifestations of the two forms are similar, except that cyanosis is likely to be more intense in the secondary form, mild or severe ocular manifestations may be associated with either type.

The following case is here presented as an example of the secondary form of polycythemia, or erythrocytosis, which resulted from a toxic

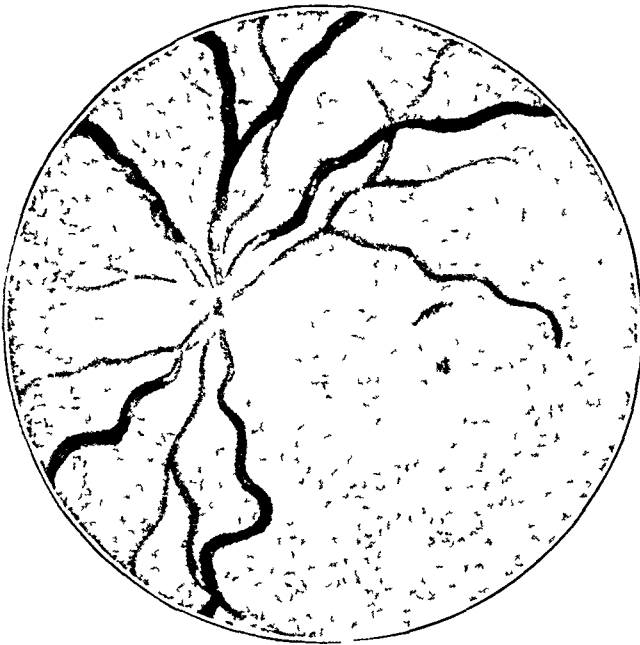


Fig 1—Fundus (left) in a case of erythrocytosis

process, the patient had sudden impairment of vision in the left eye, with a hemorrhage and edema in the macular region.

H. S., aged 37, was employed as a supervisor in a zinc-refining plant. He first came under observation Feb. 12, 1945 because of rather sudden impairment of vision in the left eye, with a resulting acuity of 20/100. There was a small paracentral scotoma in the left eye. External examination revealed practically a normal condition. Ophthalmoscopic examination of the left eye showed that the media were clear, the optic nerve head was somewhat blurred in outline. Just above the macula was a small, apparently recent, superficial hemorrhage, which was accompanied with an area of edema extending downward toward the macula. The retinal veins were distended and bluish, while the arteries had a somewhat bluish purple appearance. No other lesions were observed. Examination of the right eye revealed no hemorrhages or other pathologic change except a distention of the retinal veins and a bluish color of both arteries and veins.

² Cohen, M. Lesions of the Fundus in Polycythemia. Report of Cases, *Arch. Ophth.* **17**: 811 (May) 1937.

Examination of the nose, throat, sinuses and teeth showed nothing abnormal. Examination by Dr Benjamin Gouley revealed that the heart was normal and the electrocardiogram not remarkable. On fluoroscopic examination the heart appeared to be of approximately upper normal size. The pulsations were regular and of fair amplitude, and there was no evidence of pulmonary congestive failure. The urine showed a trace of albumin. The prostate gland was normal. The Wassermann reaction was negative. The blood pressure was 130 systolic and 90 diastolic. There was no evidence of cardiac failure. The liver was moderately enlarged, the lower border being palpable 3 fingerbreadths below the right costal margin in the midclavicular line. The lower pole of the spleen was barely palpable. The blood count showed the presence of polycythemia. The hemoglobin concentration was 106 per cent, the red cell count was 5,400,000 and the white cell count 14,400, with 74 per cent polymorphonuclear leukocytes, 25 per cent lymphocytes and 1 per cent monocytes. There was no increase of blood platelets. The differential count showed no abnormality of the white blood cells. The red cells, however, presented two interesting changes, in contrast to each other, namely, (1) the presence of full-bodied erythrocytes in large numbers and (2) the presence of many erythrocytes undergoing hemolysis, leaving narrow rims of many cells. This was interpreted by the hematologist as indicating that the erythrocytes were being destroyed while, at the same time, the bone marrow was overproducing. The hemoglobin later rose to 130 per cent, with 6,000,000 red cells. The white cell count was 11,000. The blood smear showed subsidence of peculiar destructive changes previously noted in the erythrocytes, and toxic hypoplastic anemia, although expected, did not occur. The urobilinogen level was normal. There was a slight, subclinical increase in the icterus index—10. The blood urea nitrogen was normal—14 mg per hundred cubic centimeters—as were the other chemical constituents of the blood. The hemoglobin was now reduced to 102 per cent and the white cell count to 8,000.

The patient was hospitalized and remained under treatment, with gradual improvement in his ocular and general condition. It is interesting to note that this man, who had no previous complaints and was in apparent good health, came under observation because of the visual disturbance and that the condition of the blood was discovered when he was referred for a complete physical examination. In the opinion of the hematologist, the polycythemia was an expression of a toxic process, probably a chemical intoxication, which was responsible at the same time for the intraocular hemorrhage. The toxic stimulus, however, was not severe enough to produce anemia. The enlargement of the liver was part of the process, rather than a complication of cardiac dysfunction.

The hemorrhage and edema in the left eye gradually cleared, and vision returned to normal with a correcting lens. When last seen (April 3, 1945) the patient had resumed his employment and was using a respirator mask in the plant.

THE ANEMIAS

The anemias as a group probably include the largest number of diseases of the blood, with a variety of etiologic factors, which probably have best been classified by Ottenberg.³ According to this classification, the anemias which are of greatest interest to the ophthalmologist are

3 Ottenberg, R. Reclassification of the Anemias, *J A M A* **100** 1303 (April 29) 1933.

those which result from the following conditions (1) deficiencies (a) iron deficiency (loss of blood and hypochromic anemia), (b) deficiency of the antianemic principle, as in pernicious anemia and pernicious anemia of pregnancy, (2) injury to the blood-forming organs (a) osteosclerosis, leukemias, Hodgkin's disease, Gaucher's disease, Niemann-Pick disease, Schuller-Christian disease and other disorders with lipid deposits in the bone marrow, (b) interference with regeneration of blood diseases of the spleen, such as Banti's syndrome

Most of the chronic forms of disease with disturbances or alterations in the hemopoietic system exhibit a marked progressive anemia, enlargement of the liver and spleen and a distinctive blood picture. The variety and extent of the ocular changes may be said to depend in general on the type and extent of involvement of the other structures, particularly those of the blood and the blood-forming tissues.

The ocular changes associated with the anemias include chiefly (1) changes in the appearance and size of the retinal vessels, (2) changes in the retina itself (principally pallor, hemorrhages and edema), (3) edema and swelling of the optic disks and (4) exophthalmos. The first three are characteristic especially of the primary and secondary anemias (pernicious anemia, sudden loss of blood, purpura, the leukemias and splenic anemia). Exophthalmos and displacement of the eyeball occur chiefly with lymphoma, Hodgkin's disease, lymphosarcoma and chloroma, and also with the diseases involving the bone marrow with lipid deposits in the bones of the orbit, as in Schuller-Christian disease. (In other diseases, such as Gaucher's disease and Niemann-Pick disease, which may be accompanied with mild hypochromic anemia, the ocular changes are produced by the characteristic deposits in other structures.)

The following tabulation is a brief summary of a case of pernicious anemia (hyperchromic anemia), in which large hemorrhages were present in the retina but none was observed with the so-called white center.

Pernicious Anemia (Hyperchromic Anemia)			
Mr A G	Age 55	Occupation Baker	Weight 154 lb (69.9 Kg) Admitted 10/13/45
Blood Picture		Clinical Signs	Ocular Changes
Red cells 1,890,000		Precordial pain, dyspnea, slight distention of abdomen, pallor of skin, spleen and liver not palpable, achlorhydria, digestive disturbances, edema of ankles	Optic disks round, with margins slightly blurred and slight edema around disk, retinal veins distended, arteries pale and tortuous, a few small, linear retinal hemorrhages in both eyes, fairly large hemorrhages along both superior and inferior temporal vessels, none with white center
Hemoglobin 69 Gm —48%			
White cells 5,100			
Platelets 190,000			
Sternal puncture Many megaloblasts, appearance of marked hyperchromic macrocytic anemia, compatible with diagnosis of pernicious anemia or hyperchromic anemia of other origin			
Blood pressure 110/60			
Blood sugar 120 mg /100 cc			
Urea nitrogen 18 mg /100 cc			

In cases in which the changes in the blood occur suddenly, as, for example, from severe trauma or after sudden, severe hemorrhage, changes in the retina with visual loss may follow.

A number of cases with retinal hemorrhage, exudates and loss of vision from trauma to other parts of the body have been published in the literature from time to time. Recently, Rados, Bedell and Spaeth⁴ each described a case of Purtscher's disease (angiopathy of the retina) resulting from trauma. The injury in most cases is of a crushing variety, which results in venous congestion with secondary manifestations in the cranium and changes in the retina. The latter are characterized by a retinal angiopathy, the principal features of which are engorgement of the retinal veins, retinal hemorrhages and the presence of edema and white spots in the retina. Papilledema, papillitis and large pre-retinal hemorrhages may also occur. Both eyes are usually involved. Vision may not be greatly impaired unless the macula is involved. The lesions may heal, leaving no trace of their former presence. The

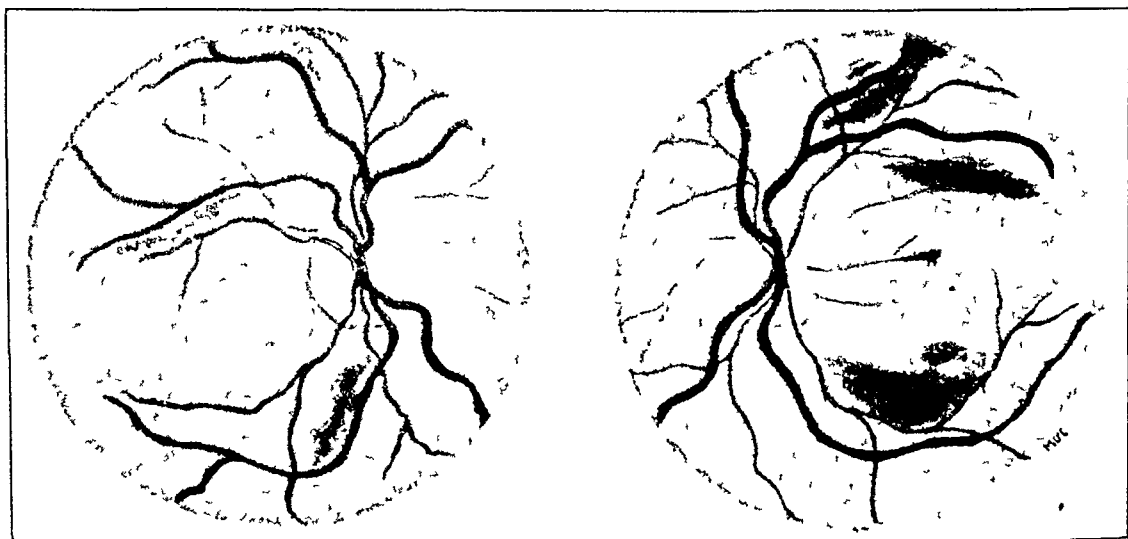


Fig 2—Fundus in a case of hyperchromic macrocytic anemia (pernicious anemia)

retinal hemorrhages may be numerous and are usually of the striate, punctate or petechial variety. They lie contiguous to the vessels but are apparently not related to the white spots.

The white spots constitute the prominent and interesting feature. They appear as bright white specks, predominantly between the disk and the macula. They frequently obscure the veins, to which they show a close relation, and have been described as resembling scattered "snowflakes" in outline and appearance. Their margins are indistinct and

4 Rados, A. Lymphorrhagia Retinae Traumatica, *Arch Ophth* 6:93 (July) 1931. Bedell, A. J. Traumatic Retinal Angiopathy, *ibid* 22:351 (Sept.) 1939. Spaeth, E. B. Traumatic Liporrhagia Retinalis (Verhoeff), Purtscher's Disease, *ibid* 31:191 (March) 1944.

are split into fine striations. They regress rapidly, diminish in number and density and dissolve into fine, silvery bright puncta and striae. The exact cause of these spots is still undetermined. It had been considered that a thrombosis of the intravascular sinuses occurs or that a sudden increase of intracranial pressure takes place, cerebrospinal fluid being forced along the vaginal sheath to produce the retinal changes. Spaeth cited Verhoeff, who stated that it is possible for fat droplets to be generally diffused in the retina, together with the presence of a generalized hemorrhagic situation in the retina, the brain or both, as a result of factors other than the emboli themselves. The name "traumatic liporrhagia retinalis" was suggested as adequately describing the condition. The appearance of the spots strongly suggested the presence of fat, and they were said to occur only where there had been fracture and obstruction of the retinal veins. They are most likely due to venous obstruction associated with traumatic hyperlipemia. Distention of the small vessels might permit the fat to pass into the tissues, either by diapedesis or through small breaks in the distended vessels. Usually some blood is extravasated with the fat.

Severe loss of blood from injury or profuse hemorrhage for any reason which results in severe anemia may be followed by temporary or permanent impairment of vision. Cox⁵ reported a case in which loss of vision followed a crushing injury to the chest. The loss of vision was attributed to anemia following massive loss of blood.

Langdon⁶ reported a case of amaurosis following severe uterine hemorrhage which lasted for long periods at a time. Examination of the eyes revealed only a "white fluffy material" covering the disks and obscuring their margins. There were no intraocular hemorrhages. The blood count showed 45 per cent hemoglobin, 1,880,000 red cells and 22,000 white cells. After treatment for several months, the disks were described as slightly pale, but otherwise the fundi were normal. Vision improved to nearly normal in each eye.

Edema of the nerve heads and choked disks have been observed in patients with different types of blood dyscrasia. A few cases of purpura hemorrhagica have been reported with choked disk in the absence of an intracranial pathologic process. The mechanism for the production of papilledema and choked disk in these cases is therefore not clear. Three such cases of thrombopenic purpura with bilateral choked optic disk and a fourth case in which choked optic disks appeared in the course of recurrent severe hemorrhages from a gastric ulcer were

⁵ Cox, R. A. Amblyopia Resulting from Hemorrhage, *Arch Ophth* **32**: 368 (Nov) 1944.

⁶ Langdon, H. M. Amaurosis After Uterine Hemorrhage with Restoration of Vision Following Transfusion, *Arch Ophth* **10** 99 (July) 1933.

reported by Watkins, Wagener and Brown⁷ It was believed that no intrameningeal or intracerebral bleeding had occurred in any of the cases and that some other factor was responsible for the occurrence of the papilledema They suggested that the mechanism of production was "a local reaction of the tissues of the optic nerves to anoxemia that resulted from loss of blood" This conclusion was based principally on the need of an adequate supply of oxygen by the retina and optic nerve to insure normal function, which is rapidly and permanently lost in even short periods of deprivation of oxygen The reduced oxygen-carrying power of the blood resulting from acute or chronic loss of blood might produce anoxemia of the tissues of the optic nerve and retina sufficient to induce papilledema and edema of the retina It would occur for the same reason in cases of angiospastic retinitis The appearance of edema of the optic nerve and retina is often observed in cases of severe anemia from any cause

LEUKEMIAS

Anemia, usually of a progressive type, is an almost constant feature of the leukemias Although typical leukemic changes in the eye are described under the designation of "leukemic retinitis," the ocular manifestations may show variations, and only part of the usual picture may be observed, especially in the early stages The most constant, and probably the earliest, evidence in the eyes in leukemia are the changes in the appearance, caliber and tortuosity of the veins, which become dilated, tortuous and darker than normal A pinkish yellow color of the fundus, the appearance of some edema of the optic disks and retinal hemorrhages are the other important changes

Gibson⁸ in a report of the retinal changes in 22 cases of leukemia, attached great significance to these changes in the retinal veins, since they are nearly always present, even when hemorrhages are not seen His observations showed that the changes in the retinal veins, with the presence of the retinal hemorrhages, is so characteristic of leukemia as to point to the diagnosis This sign is even enhanced when a narrow white line is observed on each side of the vein, indicating perivenous infiltration

The significant ocular changes in the leukemias were also described by Goldbach,⁹ who attributed the changes in the caliber and tortuosity of the veins to the altered blood picture He stated that edema of

7 Watkins, C H , Wagener, H P , and Brown, R W Cerebral Symptoms Accompanied by Choked Optic Discs in Types of Blood Dyscrasia, *Am J Ophth* **24** 1374 (Dec) 1941

8 Gibson, G G Clinical Significance of the Retinal Changes in Leukemia, *Arch Ophth* **20** 364 (Sept) 1938

9 Goldbach, L J Leukemic Retinitis, *Arch Ophth* **10** 808 (Dec) 1933

the retina is produced secondarily to the retarded blood flow, especially in the veins and capillaries, which results in seepage of the blood elements from the capillaries with secondary pressure on the perivascular lymph sheaths. The yellow to light pink color of the fundus in leukemic retinitis was attributed to the degree of infiltration of the choroid, the condition of the retinal circulation and the type and location of the hemorrhages. The lymphatic obstruction, retarded circulation, dilated and tortuous veins, extravasation of plasma and relatively unyielding lamina cribrosa tend toward local edema and congestion of the disk.

The size and shape of the hemorrhages may vary from small, narrow streaks to massive areas in the more pronounced cases. The typical hemorrhage of leukemic retinitis, with its so-called white center, is not always in evidence. It is also true, as was stated by Goldbach, that the hemorrhages are not characteristic of any of the various types of the disease. The amount of hemorrhage in the retina also seems to be proportional to the degree of anemia and bears no relationship to the number of white cells. This is in accord with the observations of both Goldbach and Gibson.

The summaries of 4 cases are here presented. They include 2 cases of chronic myelogenous leukemia, 1 case of subacute lymphatic leukemia (aleukemic phase) and 1 case of osteosclerosis with aleukemic leukemia, including a summary of the blood picture, clinical signs, ocular changes and autopsy observations in 2 cases. One of the 2 cases of chronic myelogenous leukemia is of interest because of the fact that although the anemia was comparatively moderate a number of retinal hemorrhages with moderate edema and distended veins were present. The second case was that of a woman aged 27 who died after an illness of more than two years. She had anemia of about 50 per cent, but the ocular changes during the terminal stages of the disease consisted only of moderate distention of the retinal veins, with no retinal hemorrhages in either eye.

CASE 1—*Chronic myelogenous leukemia*

Mrs. O. d. A. Age 47 Height 5 ft 3 in (167 cm), Weight 213 lb (96.6 Kg)
Admitted 12/26/44 Discharged 2/1/45

Blood Picture	Clinical Signs	Ocular Changes
Red blood cells 3,190,000-3,220,000	Patient complained of poor vision	Optic nerve heads blurred, surrounded with edema,
Hemoglobin 92 Gm—64%	Splenomegaly, hepato	retinal veins engorged and
98 Gm—68%	megaly, distended ab	tortuous, superficial retinal
95 Gm—66%	domen	hemorrhages and large pre
12/26/45 2/1/45	Weight, 256 lb in Aug	retinal hemorrhage with yel
White blood cells 250,000 110,000	1944	lowish center in left eye
Roentgen therapy—January 1945	Blood pressure, 114/78	
9/5/45 9/18/45		
White blood cells 50,000—80,000	Blood sugar, 90 mg /100 cc	
Red blood cells and hemoglobin unchanged	Wassermann and Kahn reactions of blood negative	

CASE 2—*Chronic myelogenous anemia*

Mrs J C Age 27 Blood pressure 130/90 Four previous admissions
Admitted 5/22/45 Died 8/2/45

Blood Picture				Autopsy (1 Hr After Death)	Ocular Changes
	5/22	6/4	7/30		
Red blood cells	2,750,000		2,400,000	Chronic myelogenous leukemia with leukemic infiltration of all organs	No typical evidences of leukemia except moderate congestion of central retinal veins
Hemoglobin	81 Gm	105 Gm	725 Gm	Spleen 2,840 Gm	
	56%	70%	50%	Liver 3,160 Gm	
White blood cells	43,000	70,000	60,000	Blood Wassermann reaction negative, Rh negative	
6/7/45 White cells, 4,900 after intravenous injection of 10 cc of radioactive phosphorus (strength, 10 millicuries)					
Myeloblasts 76-80% at death					

The patient with subacute lymphatic leukemia, a 19 year old student, had marked anemia, and examination of the eyes showed edema of the nerve heads, distended retinal veins and a number of preretinal hemorrhages in both eyes. The hemoglobin concentration ranged from 22 to 30 per cent, and the red cells, from 1,200,000 to 1,700,000.

CASE 3—*Subacute lymphatic leukemia (aleukemic phase)*

A M Student, Age 19 Admitted 10/7/40 Died 12/7/40

Blood Picture	Clinical Signs and Autopsy Observations	Ocular Changes
Hemoglobin 49.31 Gm	Weakness, pallor cervical axillary and inguinal lymphadenopathy	Margins of disks fairly well outlined in both eyes, retinal veins congested, four or five preretinal hemorrhages in each eye
34%-27%	Autopsy Spleen Hyperplasia	one smaller retinal hemorrhage with white center in right eye
Red blood cells 1,740,000 1,200,000	Liver Cloudy swelling, amyloid degeneration fatty change, congestion, edema	
White blood cells 1,300 2,900	Bone marrow Congestion, fibrosis, leukemic cell infiltration	
Platelets 80,000		
Coagulation time 5½ min		
Bleeding time 11 min		
Sternal puncture Marrow counts support diagnosis of subacute lymphatic leukemia in aleukemic phase (counts unchanged until death)		
Blood pressure 115/58		
Blood sugar 104 mg/100 cc		
Urea nitrogen 112 mg/100 cc		
Wassermann and Kahn reactions negative		

The patient with osteosclerosis and aleukemic leukemia, a man aged 51, complained of weakness, vertigo and swelling of the abdomen and ankles. He was jaundiced, the liver and spleen were greatly enlarged, and there was a large mass on the right side which was thought to be the liver. Roentgenographic examination revealed diffuse osteosclerosis of the bones of the spine, shoulder girdle and long bones. A subacute hyperplastic lymphadenitis was present. There was an anemia of somewhat less than 50 per cent. The eyes showed anemia of the retina and edema of the optic disks. The retinal veins were distended, but no hemorrhages were observed.

CASE 4—*Osteosclerosis with aleukemic leukemia*

Mr D L Age 51 Admitted 6/16/45 Discharged 8/14/45

Blood Picture	Clinical Signs and Biopsy Observations	Ocular Changes
Red blood cells 2,430,000 2,810,000	Liver and spleen enlarged	Blurred nerve heads with moderate edema in retina
Hemoglobin 50.54%	all bones of chest, dorsal part of spine and long bones showed evidences of osteosclerosis	around disks, congested veins, arteries pale no hemorrhages or exudates
White blood cells 5,800 10,500	Biopsy of inguinal lymph nodes showed hyperplastic lymphadenitis	
Blood sugar 109 mg/100 cc		
Urea nitrogen 27.8 mg/100 cc		
Wassermann reaction negative		

BANTI'S SYNDROME

This disease is characterized by an enlarged spleen, a tendency toward gastric hemorrhage, epistaxis, cirrhosis of the liver with ascites, especially in the later stages, and progressive anemia. Although the cause of the condition is obscure, it is known that venous congestion of the spleen takes place, associated with cellular proliferation. The anemia is also unexplained except that direct loss of blood from hemorrhage may be a factor. The early anemia of the disease may be due to splenic dysfunction, without any evidence of a direct destructive action by the spleen or of any definite toxic or hemolytic agent. Hypochlorhydria or achlorhydria usually occurs.



Fig 3—Fundus in a case of anemia associated with osteosclerosis and aleukemic leukemia

The following case of Banti's syndrome with autopsy is of particular interest because of the pronounced changes in both eyes and because no case of this disease has been found in the literature in which ocular manifestations are described.

W. B., a 4 year old boy, had been ill for two years under the care of Dr. Eugene Rush, at Mount Sinai Hospital, Philadelphia. The ocular changes were observed during the last week of the disease.

The clinical signs and symptoms included early loss of weight, pallor of the skin, cachexia and moderate jaundice. Gastric hemorrhages and epistaxis occurred both early and late in the disease. The abdomen was greatly distended with ascites, and abdominal paracentesis was performed several times. The liver and spleen were greatly enlarged.

Examinations of the blood revealed hemoglobin values of 48, 50, 56 and 32 per cent. The red cell count was 2,000,000. There was a prothrombin deficiency of 28 per cent.

Ophthalmic Examination—The sockets were deep, and there was a pale conjunctiva with moderate jaundice in both eyes but no other external abnormalities of note. Ophthalmoscopic examination revealed that the media were clear in each eye. The optic disks were blurred in outline and showed considerable edema. The retinal veins were greatly distended, and the arteries were pale. There were also a marked pallor and moderate edema of both retinas. A number of round and linear, superficial hemorrhages were seen in the retina of each eye close to the disk and also in the periphery. Many of these hemorrhages surrounded a white center and were similar to those which occur in leukemic retinitis. In the left eye there were also a number of small, yellowish white areas of infiltration around the macula. Since Banti's syndrome is not a distinct entity and there are no specific pathologic changes which identify the disease, the changes in the optic nerves, retinas and retinal vessels in this case can be attributed to the severe anemia which was present.

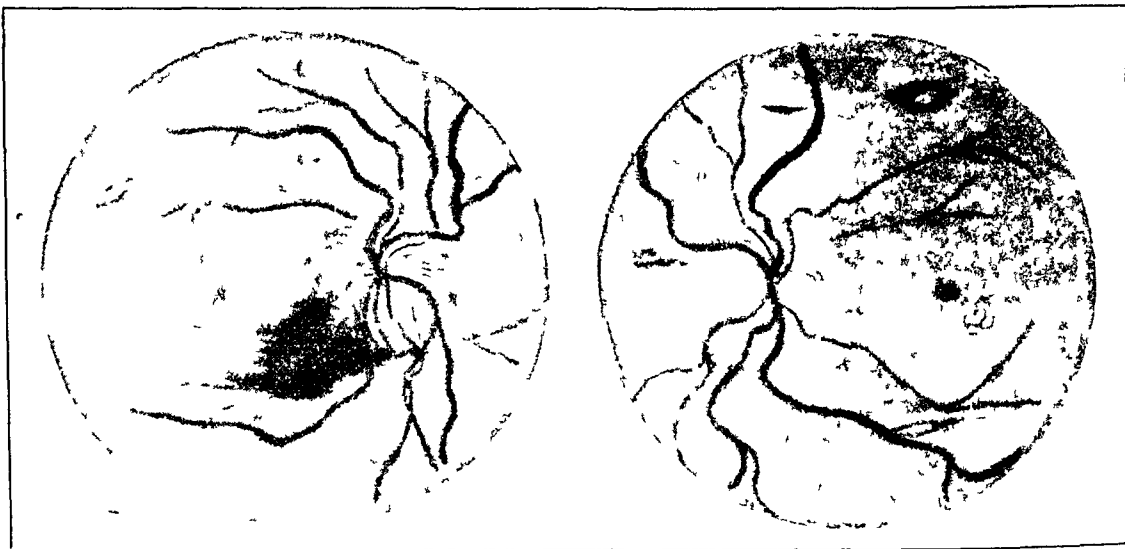


Fig 4—Fundus in a case of Banti's syndrome (splenic anemia) with severe anemia

Autopsy, by Dr David Meranze, pathologist, Mount Sinai Hospital, confirmed the clinical diagnosis. The appearance of the spleen was compatible with Banti's syndrome. There were cirrhosis of the liver, marked hemorrhage into the pulmonary alveoli and bilateral pleural effusion.

OTHER BLOOD DYSCRASIAS

Exophthalmos is probably the most prominent clinical sign in cases in which lymphoma occurs in the orbit. The following types of lymphomas were described by Leinfelder and O'Brien¹⁰ (1) sclerosing (Hodgkin's disease), (2) endothelial (lymphoendothelioma), (3) lymphoblastic (lymphosarcoma) and (4) lymphocytic (lymphatic leukemia). These lesions are closely related and are characterized by hyperplasia and metaplasia of the lymphoid and blood-

¹⁰ Leinfelder, P. J., and O'Brien, C. S. Lymphoma of the Eye and Adnexa. Report of Thirteen Cases, *Arch Ophth* **14** 183 (Aug) 1935.

forming tissues, with enlargement of the lymph nodes, spleen and liver and changes in the bone marrow. The blood picture is typical only in lymphatic leukemia, whereas the white cells are usually normal in the other types. In the latter, however, secondary anemia occurs, especially in the later stages of the disease. Except in lymphatic leukemia, the ocular changes in this group are rare. Nodular thickening of the lids with lymphomatous infiltration of the eyes and lids and unilateral or bilateral exophthalmos may occur. Leinfelder and O'Brien¹⁰ observed exophthalmos as a result of lymphomatous infiltration of the orbit in 6 cases.

A case of lymphoma of the orbits which was considered to be associated with chronic lymphatic leukemia was reported by Cohen¹¹ in a man aged 65 with bilateral exophthalmos. The laboratory diagnosis of leukemic growth was made after removal of the growth.

Chloroma is a rare condition characterized by the presence of a neoplastic tumor of the orbit, with exophthalmos probably the most prominent ocular finding. The tumors are typically green in color and occur in association with involvement of the hemopoietic tissues and a leukemic blood picture. A case occurring in a man aged 55 with bilateral exophthalmos was reported by Gump, Hester and Lohr.¹² In this case the blood picture was one of monocytic leukemia and pathologic involvement of the reticuloendothelial system. Another case of the disease occurring in a 4 year old boy with exophthalmos of the left eye was reported by Frost,¹³ who stated that the underlying pathologic process reveals that the disease is a particular type or an unusual form of myelogenous leukemia.

The prominent ocular manifestation in Schuller-Christian-Hand disease is exophthalmos, usually bilateral. The other characteristics of this syndrome are degeneration and lipid deposits in the bones, especially the bones of the skull and orbit, and diabetes insipidus. The disease is congenital and familial in origin and is peculiar to male children, and the pathologic changes involve the reticuloendothelial system. The liver, spleen, lymph nodes and kidney are moderately enlarged. A severe anemia occurs, with extensive involvement of the bone marrow.

SUMMARY

The blood dyscrasias are a group of diseases characterized by various alterations in the circulating cellular constituents, which accompany abnormal processes in other tissues.

11 Cohen, M. Orbital Lymphoma in Chronic Lymphatic Leukemia. Report of a Case, *Arch Ophth* **11** 617 (April) 1934.

12 Gump, M. E., Hester, E. G., and Lohr, O. W. Monocytic Chloroma, *Arch Ophth* **16** 931 (Dec) 1936.

13 Frost, A. D. Chloroma. Report of a Case with Hematologic Study, *Tr Am Acad Ophth* **42**:123, 1937.

A case of erythrocytosis with ocular changes, which was probably toxic in origin and was of temporary duration, is described

The anemias are classified, and those diseases with ocular changes in which the anemia is an important factor are described. A case of hyperchromic anemia (pernicious anemia) with ocular changes is presented

The ocular changes in the leukemias are described, with reference to the literature. Four cases of leukemia with their ocular changes are summarized

A case of Banti's syndrome (splenic anemia) with profound anemia and marked changes in the retinas and both optic nerves is presented. These ocular changes were probably the result of the anemia

CONCLUSIONS

Most of the diseases included among the blood dyscrasias are accompanied with anemia of various types and degrees. The ocular changes occurring in these diseases may involve principally the optic disk, retinal vessels and retina in the form of edema, hemorrhages and venous distention. The degree of anemia present may in general be said to determine the type and extent of the ocular involvement

Exophthalmos is the prominent ocular manifestation in those diseases in which the abnormal process occurs in the orbit or involves the bones of the orbit

DISCUSSION

DR PAUL REZNIKOFF, New York. It is not generally realized that patients do not go to a hematologist directly—they are sent to him by another physician. A blood dyscrasia is usually suspected by the ophthalmologist, the dentist or the dermatologist, or by an internist occasionally, but the patient practically never says, "I have something wrong with my blood so I am going to a hematologist." Therefore it is important for specialists, such as ophthalmologists, to recognize conditions which may be due to a hematologic condition. This brings me to the point which hematologists are always stressing, that the hematologic findings in cases such as those presented by Dr. Tassman must be correlated with the entire condition of the patient, as he has done. In a general way, there is no such thing as a primary blood disease. All disorders of the blood are secondary. That is why hematologists have dropped the classification of primary and secondary anemias. The so-called pernicious anemia is not primary, for it is due to a deficiency in a nutritional factor. Such a blood dyscrasia as leukemia, for example, is considered primary because the cause is not known. If it were known, the disease would not be called primary.

Sulfonamide therapy has introduced many hematologic conditions, some of which are fatal, and the same is true of thiouracil, which is used for hyperthyroidism and has produced several cases of agranulocytosis. Fatal cases of purpura may result from gold salt therapy in the treatment of arthritis.

One type of anemia which I did not see in Dr Tassman's classification, and one which is important for the ophthalmologist, is hemolytic anemia. This frequently results in hemorrhages in the retina, surprisingly, often the first evidence of hemolytic anemia is found by the ophthalmologist, who notes jaundice of the sclera, occasionally missed by the clinician, especially if his office has artificial illumination.

As one may gather from Dr Tassman's report, with the possible exception of leukemia, there is practically no blood disease for which the changes in the eye are pathognomonic—so that one can say that the patient has polycythemia, or so-called Banti's syndrome, or anemia. What can be gathered from the ophthalmic examination is that something may be amiss with the bleeding or clotting mechanism, and in the further investigation of these factors a hematologic study is indicated.

I do not know of any case of hemophilia in which a so-called non-traumatic, or spontaneous, hemorrhage involved the eye. If such a patient is struck in the eye, he will bleed, but few hemophilic patients have had "spontaneous" hemorrhages. That is not true of hemorrhages in other sites. For the normal patient, the trauma is of minimal significance, and he repairs the damage rapidly, but the hemophilic patient cannot. I suspect from the fact that there are so few reports of so-called spontaneous hemorrhage in orbital structures that trauma caused by the ordinary movement of the eyeball is rare. The eye is well protected from trauma, such as occurs to the knee or other joints. Even in the urinary tract the passage of urine produces some trauma, and hemophilic patients may bleed profusely from the urinary tract.

One of the problems encountered with polycythemic patients, and one not yet solved, is hemorrhage in the retina, which causes a great deal of disturbance. However, it is generally considered that patients with this disease have a rather sluggish circulation, which is conducive to thrombosis of the veins, they also have a high red blood cell count, so that the plasma has little room for clot retraction.

My final remark has to do with hemorrhages in the hematologic conditions, which Gibson has indicated may be due to anemia. That is puzzling to hematologists, because in even the severest anemias hemorrhage is not so frequent as in a condition like thrombopenic purpura, with little anemia, or in leukemia, with only moderate anemia. It is my impression that if Gibson could repeat his studies, and correlate hemorrhage not only with the white blood cell count and anemia but with the platelet count as well, he might find that most of the hemorrhagic conditions in the eye are due to thrombopenia. Hemorrhage is very common in leukemia, especially of the acute type, and in the so-called aplastic anemia, and, as can be seen from Dr Tassman's tables, it is not uncommon to have some degree of thrombopenia in pernicious anemia, as well as in so-called Banti's syndrome.

DR RUDOLF AEBLI, New York. In my own experience in the last two years I have had 2 cases in which expulsive choroidal hemorrhage followed cataract extraction. Subsequently, I found that both the patients had polycythemia vera.

OCULAR SPOROTRICHOSIS

Report of a Case

DAN M GORDON, M D

NEW YORK

SPOROTRICHOSIS is a widespread but relatively uncommon disease

The condition is not figured by Smith in his *Atlas of Skin Diseases in the Tropics*, nor does Loewenthal mention it in his account of the diseases of the Skin in negroes ¹

Most of the reported cases have come from France and the United States. Isolated cases have been reported in Germany, Switzerland, Austria, Belgium, England, Scotland, China, Turkey, Italy, Spain, Madagascar, where it is rather common, and South America. Three large series of cases have been described among South African miners ²

Du Toit ^{2b} stated that only 206 cases had been reported in the American literature up to January 1940. Link in 1809, cited by Moore and Kile,³ described the genus *Sporotrichum* chiefly as a saprophyte on wood. *Sporotrichum badium* was the first species described and illustrated. The first pathogenic species was probably that described by Montagne, in 1886. Schenck ⁴ in 1898 described the first case, in which a typical lesion occurred on a finger, followed by the formation of a chain of nodules. This observer did the first scholarly work on sporotrichosis. He recovered the organism twice in cultures. The organism was classified by E. F. Smith, of the United States Department of

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Read in part at a meeting of the New York Academy of Medicine, Section of Ophthalmology, May 21, 1945. A brief abstract of this paper, with discussion, appeared in the November-December 1945 issue of the *ARCHIVES*, page 463.

1 Dangerfield, L. H., and Gear, G. Sporotrichosis Among Miners on the Witwatersrand Gold Mines, *South African M. J.* **15** 128, 1941.

2 (a) Dangerfield and Gear ¹ (b) du Toit, C. J. Sporotrichosis on the Witwatersrand, *Proc. Transvaal Mine M. Officers A.* **22** 111, 1942. (c) Piiper, A., and Pullinger, B. D. An Outbreak of Sporotrichosis Among South African Native Miners, *Lancet* **2** 914, 1927.

3 Moore, M., and Kile, R. L. Generalized, Subcutaneous, Gummatous, Ulcerating Sporotrichosis, *Arch. Dermat. & Syph.* **31** 672 (May) 1935.

4 Schenck, B. T. On Refractory Subcutaneous Abscesses Caused by a Fungus, Possibly Related to the *Sporotricha*, *Bull. Johns Hopkins Hosp.* **9** 286, 1898.

Agriculture, as belonging to the genus *Sporotrichum*, which had been created by Link in 1809 Mount⁵ stated

Great credit is due Schenck, for as a result of his research there was added to dermatology the description of a disease worked out completely in the United States

Brayton in 1899 described a similar case but failed to prove the diagnosis by culture⁶ Hektoen and Perkins⁶ described their case in 1900 and isolated the organism in culture Hektoen gave the name *Sporotrichum schenckii* to the fungus The first non-American case was described by de Beurmann and Ramond⁷ in 1903 In 1905 the organism was named *Sporotrichum beurmanni* by Matruchot and Ramond, cited by du Toit,^{2b} who isolated and studied the fungus

It was once thought that there was a difference between *Sporotrichum schenckii*, which had been described in the United States, and *Sporotrichum beurmanni*, described by the French Davis⁸ proved that the two were identical, with Schenck getting credit as the first observer It would seem, then, that it would be more correct historically and as a matter of custom to refer to the organism as *Sporotrichum schenckii* Actually, the literature contains both terms, to the confusion of the reader

In 1907 Danlos and Blanc⁹ published the first case in which sporotrichosis had been known to involve the eye or its adnexa Here the lid was involved The same year de Beurmann, Gougerot and Laroche,¹⁰ whose names are so firmly linked to the history of sporotrichosis, also cited a case of involvement of the lid Greco¹¹ reported a similar case from the Argentine in the same year

In 1908, 2 cases were reported from France—a case of infection of the lid, by Morax and Carlotti,¹² and a case of orbitopalpebral involve-

5 Mount, L B Sporotrichosis, with Report of a Rather Unusual Case, Arch Dermat & Syph **25** 528 (March) 1932

6 Hektoen, L, and Perkins, C F Refractory Subcutaneous Abscesses Caused by *Sporothrix Schenckii*, J Exper Med **5** 77, 1900

7 de Beurmann and Ramond Abscès sous-cutanés multiples d'origine mycosique, Ann de dermat et syph **4** 678, 1903

8 Davis, D J Interagglutination Experiments with Various Strains of *Sporothrix*, J Infect Dis **12** 140, 1913, The Formation of Chlamydospores in *Sporothrix Schenckii*, ibid **15** 483, 1914, The Effect of Potassium Iodid on Experimental Sporotrichosis, ibid **25** 124, 1919

9 Danlos and Blanc Un cas de sporotrichose palpebrale, Bull et mém Soc méd d hôp de Paris **24** 1450, 1907

10 de Beurmann, Gougerot, and Laroche Gomme de la paupière, Bull et mém Soc méd d hôp de Paris **27** 1046, 1907

11 Greco, O Sporotrichose linfangitica nodular vegetante, cited by Bedell³⁵

12 Morax, V, and Carlotti, P La sporotrichose palpébrale, Ann d'ocul **139** 418, 1908

ment, by Fage¹³ In 1909, 6 cases appeared in the French literature Thibierge and Gastinel¹⁴ cited a case of involvement of the lid Morax¹⁵ had a case of conjunctival infection Fava¹⁶ reported on a laboratory infection of his own conjunctiva He accidentally got an emulsion of the organisms into his eye One-half hour later he irrigated the eye with a 1:4,000 solution of mercury oxycyanide Eleven days later he noted a foreign body sensation in the eye and observed a yellow spot on the tarsal conjunctiva The preauricular and postauricular nodes became enlarged, and a growth of the organism was obtained on culture The condition cleared up with oral use of potassium iodide over a period of two and a half months In Burnier's¹⁷ and Weill's cases the cul-de-sac was involved In Bonnet's¹⁸ case the infection was orbitopalpebral De Beurmann and Gougerot¹⁹ cited a fatal case of generalized sporotrichosis with destruction of one eye The same case was also reported by Lagoutte and Briau²⁰

Gifford St²¹ reported the first American case in 1910, and, according to him, the first in the world in which the conjunctiva was the seat of the infection However, Morax had reported a similar case the year before According to Gifford, he had seen 5 other cases of a condition which clinically appeared to be sporotrichosis, but he had been unable to recover the organism

In 1910, 5 more cases occurred in France In Gougerot and Dubosc's²² case the lid was involved Morax and Cruchadeau²³ cited a case in which the conjunctiva was invaded Velter²⁴ reported a case of orbital abscess The patient refused treatment with potassium iodide, and the lesion consequently did not heal while he was under

13 Fage, A Sur un cas de sporotrichose, *Progres méd* **24** 248, 1908

14 Thibierge, G, and Gastinel, P Trois cas de sporotrichose dermohypodermique, *Bull et mem Soc med d hôp de Paris* **26** 537, 1909

15 Morax, V La sporotrichose de l'appareil visuel, *Ann d'ocul* **141** 321, 1909

16 Fava, A Un cas de sporotrichose conjonctivale et palpebrale primitives, *Ann d'ocul* **141** 338, 1909

17 Burnier Un cas de sporotrichose gommeuse hypodermique ulcèreuse disséminée localisations conjonctivales, *Ann d'ocul* **141** 344, 1909

18 Bonnet Sporotrichose, *Lyon chir* **2** 515, 1909

19 de Beurmann and Gougerot Sporotrichose cachectisante mortelle, *Bull et mem Soc med d hôp de Paris* **26** 1046, 1909

20 Lagoutte and Briau, cited by de Beurmann and Gougerot¹⁹

21 Gifford, H Sporotrichosis of the Eye-Ball and Eyelids, *Ophth Rec* **19** 573, 1910

22 Gougerot and Dubosc Sporotrichose palpebrale, cited by Toulant⁶⁰

23 Morax, V, and Cruchadeau Sporotrichose conjonctivale primitive, *Ann d'ocul* **144** 69, 1910

24 Velter, E Un cas de sporotrichose orbito-palpebrale primitive, *Ann d'ocul* **144** 65, 1910

Velter's observation Danlos and Flandin²⁵ reported a case of de Lapersonne's²⁶ of disseminated sporotrichosis with resultant phthisis bulbi Jeanselme and Poulard²⁷ similarly reported a case of generalized sporotrichosis with involvement of the iris The patient lost his sight as a result of the exudate formed

Four more cases were published in France in 1911 Chaillous²⁸ reported a case of conjunctival infection which occurred after handling a horse with suppurating eyes Morax²⁹ told of a case in which the lacrimal sac was involved with fistula formation This patient refused treatment with potassium iodide, and there was no healing while he was under observation Legry and associates³⁰ noted a case of disseminated sporotrichosis which resulted in iridocyclitis This condition responded to iodides Doi's³¹ case was one of corneal involvement in an infant with generalized sporotrichosis following vaccination for smallpox In this case, also, the condition responded to potassium iodide

In 1912 de Lapersonne²⁶ described a case of generalized sporotrichosis in which iridocyclitis and resultant phthisis bulbi ensued The condition responded to potassium iodide, although the eye had to be removed as a result of pain The fungus was not identified in the eye, although it was observed in other tissues Chaillous²⁸ the same year reported a case of disseminated sporotrichosis with intraocular involvement and perforation of the sclera The eye was lost, although the rest of the lesions responded to potassium iodide

In 1913 Morax³² reported a case of involvement of the lid which simulated a lacrimal fistula

In 1914, 5 cases were reported Morax³³ reported a case of uveitis which was due to sporotrichosis, without other lesions The organism was recovered in a culture of the aspirated pus Thibierge and

25 Danlos and Flandin, C Sur un cas de sporotrichose traité et meconnu pendant 2 ans, Bull et mem Soc méd d hôp de Paris **29** 206, 1910

26 de Lapersonne, F Sporotrichose oculaire, Presse méd **20** 93, 1912

27 Jeanselme, E, and Poulard Sporotrichose de l'iris, Ann d'ocul **144** 65, 1910

28 Chaillous Sporotrichose conjonctivale primitive, Ann d'ocul **145** 47, 1911

29 Morax, V Sporotrichose primitive du sac lacrymal, Ann d'ocul **145** 49, 1911

30 Legry, Soudel and Velter Sporotrichose gommeuse disséminée avec lésions oculaires (iridocyclite et gommages de l'iris) et spina ventosa sporotrichosique, Bull et mem Soc méd d hôp de Paris **32** 124, 1911

31 Dor, L Un cas de sporotrichose oculaire, Clin opht **17** 121, 1911

32 Morax, V Sporotrichose primitive des paupières simulant une fistule lacrymale, Ann d'ocul **149** 183, 1913

33 Morax, V Uveite sporotrichosique avec gomme sporotrichosique épisclerale secondaire, Ann d'ocul **152** 273, 1914

Chaillous,³⁴ in France, cited a case of intraocular involvement, and the first case in which the retina was affected. There were nodules in the subcutaneous tissue and on the lid, as well as iritis. Three cases were reported from the United States in the same year. Bedell³⁵ reported a case of chronic conjunctival sporotrichosis in which six concretions were removed from the lacrimal sac. When these were cultured, after being crushed, the organism was recovered. Wilder and McCullough,³⁶ earlier that year, reported a case of the disease occurring in one of them (C P M), in which a pure culture of *Sporotrichum schenckii* was accidentally spilled into the conjunctival sac. The patient had pronounced constitutional symptoms, as well as pain and lymphangitis, but the infection responded to potassium iodide. In their discussion of this case, Dwyer and Larkin³⁷ mentioned a case of their own, never officially reported, in which an infection of the lid occurred secondary to an ulcer of the finger.

In 1917 Leoz³⁸ reported the first Spanish case, which he had seen in 1915. The patient had corneal scars and ulcers with associated submaxillary adenitis. The organism was recovered in the culture. He injected a 5 per cent solution of potassium iodide into the nodules, with good results. This author stated that before he recognized sporotrichosis he had seen a condition which in retrospect he knew to be sporotrichosis but which at the time he had called syphilis. The patient had died within two months of the diagnosis.

Oreste³⁹ reported a case of conjunctival involvement in 1919. No cultures were made in this case, and hence the diagnosis was not confirmed. The patient responded to potassium iodide.

In 1920 Alom and Vallin⁴⁰ published a case of involvement and perforation of the frontal bone, together with an abscess of the upper lid. This condition also responded to potassium iodide.

In 1921 Gonzalez⁴¹ reported an interesting case in which the disease had gone on for four years, with orbital involvement. He

34 Thibierge and Chaillous. Sporotrichose palpebrale, *Clin opht* **20** 126, 1914.

35 Bedell, A J. A Case of Chronic Sporotrichosis of the Eye, *Tr Am Ophth Soc* **13** 720, 1914.

36 Wilder, W H, and McCullough, C P. Sporotrichosis of the Eye, *J A M A* **62** 1156 (April 11) 1914.

37 Dwyer and Larkin, in discussion on Wilder, W H. Ocular Sporotrichosis, abstracted, *Arch Ophth* **45** 162, 1914.

38 Leoz, G. Esportricosis ocular, *Arch de oftal hispano-am* **17** 293, 1917.

39 Oreste, A. Sporotricosi congiuntivale, *Gazz med napol* **2** 326, 1919.

40 Alom, H, and Vallin, H G. Osteite perforante du frontal par sporotrichose, *Lyon med* **129** 859, 1920.

41 Gonzalez, J de J. Mycotic Tumor of Orbit, abstracted, *Am J Ophth* **5** 244, 1922.

finally obtained a smear showing the organism, and with potassium iodide therapy even the exophthalmos cleared. No culture was made here.

In 1922 Sobly Bey,⁴² of Egypt, reported a case which he thought was one of sporotrichosis of the inner canthus. However, the cultural characteristics of the organism differed from those of *S. schenckii*. The patient was cured with potassium iodide.

In 1922 Sanford Gifford⁴³ reported a case of involvement of the lacrimal sac with fistula formation and infection of the ethmoid sinuses. The patient required an intranasal exenteration of the ethmoid cells, with local applications of trichloroacetic acid, administration of potassium iodide and local use of iodine, before the condition cleared up. This was the first true case of dacryocystitis due to *Sporotrichum* since Morax' case, reported in 1911.²⁹ Gifford noted 2 other cases in which sporotrichosis was suspected but in which the cultures were negative.

In 1924 Sanford Gifford⁴⁴ reported a case of infection of the lid which responded to potassium iodide and local application of iodine. It is significant that the name Gifford is associated with 3 of the 9 American cases reported prior to this paper.

In 1927 King⁴⁵ cited a case of generalized sporotrichosis in which a lid was secondarily involved. This patient responded slowly to treatment with potassium iodide until large doses were given intravenously, combined with roentgen irradiation.

In 1928 Alvis⁴⁶ reported the eighth American case, that of a patient who had previously had trachoma, of eight years' duration. He noted a linear excoriation of the conjunctiva, filled with a cheesy material. Scrapings of this, when cultured, yielded a growth of the organism.

In 1930 Hill⁴⁷ reported the ninth American case, and the last one published in this country prior to the present case. Hill's case was a most interesting one. The onset was with a small nodule on the upper lid, which another physician had opened, with a diagnosis of chalazion. It grew over a period of five years, gradually involving the globe, with formation of a hypopyon ulcer and involvement of the malar and frontal bones. Radical emptying of the orbit and removal of an antral wall had to be resorted to. Three months later a small

42 Sobly Bey, M. A Case of Palpebral Sporotrichosis, *Tr Ophth Soc U Kingdom* **42** 388, 1922.

43 Gifford, S. Ocular Sporotrichosis, *Arch Ophth* **51** 540 (Nov.) 1922.

44 Gifford, S. R. Further Note on Ocular Sporotrichosis, *Arch Ophth* **53** 264, 1924.

45 King, H. Sporotrichosis with Report of an Unusual Case, *South M J* **20** 541, 1927.

46 Alvis, B. Y. Sporotrichosis of Eyelid, *Am J Ophth* **11** 381, 1928.

47 Hill, H. F. Sporothrix Infection of the Eye and Adnexa, *Tr Am Acad Ophth* **35** 128, 1930.

nodule was removed from the canine fossa. The patient was reported as cured five months later. This is the second American case in which the lesions failed to respond to iodides alone.

In 1930 Amias⁴⁸ reported a case of sporotrichosis of the bulbar conjunctiva. The condition occurred in a young boy who had scratched his eye with a chestnut twig. This was followed by the development of a punched-out ulcer and associated lymphangitis, as well as constitutional symptoms. The organism was recovered in culture, and the lad responded to treatment with potassium iodide over a period of two months.

In 1931 Fonseca⁴⁹ reported a case of sporotrichosis of the lower palpebral border. Here, again, the organism was recovered in the culture, and potassium iodide produced a cure in three months.

In 1936 Fazakas,⁵⁰ of Germany, reported a case of sporotrichosis occurring in the lacrimal canal of a patient who had had the lacrimal sac removed nine years before. Potassium iodide produced a cure here.

In 1937 Cavallacci⁵¹ cited the case of a man who had been struck in the left eye with a willow branch. Fifteen days later a small gray spot developed at the limbus. This gradually grew, although vision was not affected. The culture revealed the true diagnosis, and treatment with iodides locally and orally effected a cure within one month.

In 1939 Mendes de Castro and Amato⁵² cited a case with involvement of the cornea.

In 1940 Decoud and Schujman⁵³ reported a case of involvement of the lid, which responded to potassium iodine.

In 1941 Dangerfield and Gear¹ reported on 74 cases of sporotrichosis occurring in miners in South Africa. In 2 of these cases the infection was primary on the lid and responded to iodides.

In 1943 Nino⁵⁴ cited a case of mycotic ulcer of the cornea which he thought was due to sporotrichosis.

48 Amias, V. Un caso de esporotricosis de la conjunctiva bulbar, *Arch de oftal hispano-am* **30** 644, 1930, abstracted, *Am J Ophth* **14** 845, 1931.

49 Fonseca, A. Oculopalpebral Sporotrichosis, *Rev de oftal de São Paulo* **1** 33, 1931, abstracted, *Am J Ophth* **15** 479, 1932.

50 Fazakas, A. Sporotrichose des unteren Tranenkanalchens, *Klin Monatsbl f Augenh* **96** 227, 1936.

51 Cavallacci, G. Granuloma del limbus da Sporotrichum, *Arch di ottal* **44** 247, 1937, abstracted, *Arch Ophth* **20** 660 (Oct) 1938.

52 Mendes de Castro, M., and Amato, G. G. Sporotricose. Uma localização interessante, *Gaz clin* **37** 306, 1939.

53 Decoud, A. C., and Schujman, S. Esporotricosis palpebral, *An argent de oftal* **1** 422, 1940, abstracted, *Am J Ophth* **24** 1332, 1941.

54 Nino, F. L. Úlcera micótica de cornea. Estudio micológico de una observación, *Prensa med argent* **30** 797, 1943.

In this same year Bolanos and Tiejós⁵⁵ reported 2 cases of multiple facial lesions, which included the lids and which responded to iodides

In 1942 du Toit^{2b} reported on 650 cases of sporotrichosis occurring among 2,500 employees in a mine in South Africa. Although this author gave an excellent review of the subject of sporotrichosis, he failed to analyze his cases from the point of view of anatomic localization. Nor do any of his 37 pictures indicate lesions of the eye or its adnexa. He did state that "practically the only type seen on the face" occurred as a warty growth on the forehead between the eyes.

REPORT OF CASE

Mrs. M. H., a housewife aged 48, came to the eye clinic of the New York Hospital on May 1, 1944, complaining of a "sore" on her left upper eyelid. She stated that she had had this for about two weeks but could give no definite history of trauma. There were pronounced swelling and redness of the lid, with a granulomatous ulcer in the center. The ulcer was covered with a crust, under which there was considerable purulent material. The skin adjacent to the lesion was fixed. Vision was 20/15 in each eye. Examination of the eyes themselves and of the lacrimal apparatus revealed nothing pathologic. General physical examination also showed an essentially normal condition.

On the third day there was a hard nodular swelling on the lid just temporal to the ulcer. On the fifth day the reaction at the site of the original lesion was still intense, but there were now two small, pea-sized nodules temporal to the ulcer. One of these was just at the external canthus. By the ninth day enlargement of several of the nodules draining the left upper lid was noted. The skin overlying these nodules was red and indurated. An agar culture of material taken at this time was later reported to show no growth.

The patient returned again on May 12, by which time sporotrichosis was suspected. Further questioning elicited the statement that she had been working in her garden, among poinsettias, about a week prior to the onset of the "stye" on her lid. She could recall wiping the back of her soiled hand across the left supraorbital region. A culture on Sabouraud's medium was made by Dr. George Lewis of material taken from one of the nodules by aspiration. This was reported (by Miss Mary Hopper) to show a growth of *S. schenckii* five days later. At the same time an intracutaneous test with sporotrichin was performed by Dr. M. B. Sulzberger. At this visit the skin over the nodules was more inflamed than before. The nodules were of a hard, rubbery consistency and extended in a chain toward the left ear. The node at the external canthus was now becoming larger, softer and somewhat heart shaped. There was a palpable preauricular lymph node.

Two days later the intracutaneous test gave a positive reaction, with a papule 5 by 5 mm. in size, surrounded by an area of erythema measuring 22 by 30 mm. The patient stated that the reaction had been much greater on the day before.

On the sixteenth day another culture on Sabouraud's medium was made by Dr. Lewis and Miss Hopper, this, too, was reported to show a growth of *S. schenckii* four days later. At this visit the patient complained of some pain in the left supraclavicular region, and a postauricular node was palpable.

⁵⁵ Bolanos, L., and Trejos, A. Múltiples coincidencias en dos casos de esporotricosis facial, *Rev. méd. Costa Rica* 5:369, 1943.

Treatment with a saturated solution of potassium iodide was started on the twentieth day of the disease. My colleagues and I had purposely not started this medication sooner, as we were anxious to secure at least one positive culture before so doing. The initial dose was 10 drops four times daily. This was gradually increased to 15, then to 20 and by the thirty-first day to 25 drops four times daily.

Five days after the institution of the potassium iodide therapy the initial lesion had begun to involute, but the nodules had now become painful and the overlying skin angry looking. The pain radiated down the left arm. The pre-

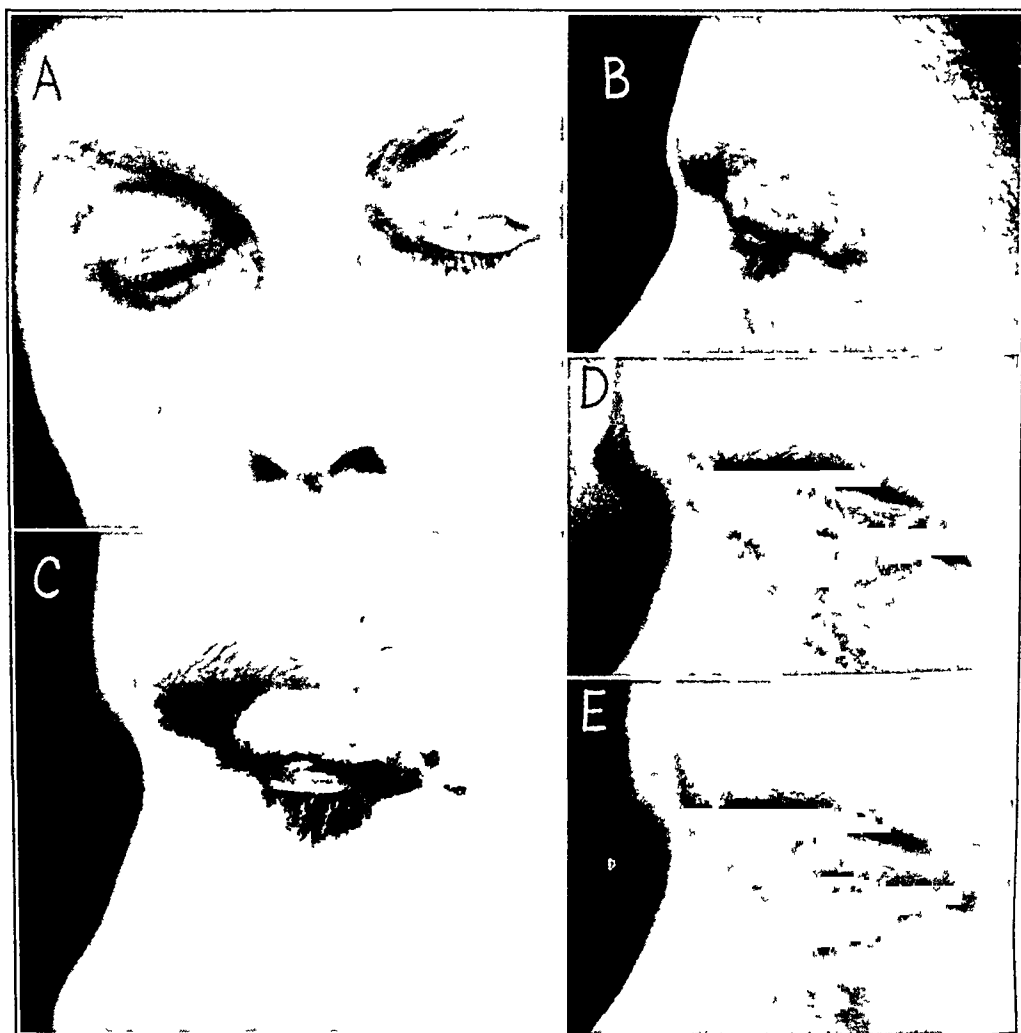


Fig 1—*A*, sporotrichosis of the left upper lid as seen about the twenty-sixth day of the disease. *B*, patient about the thirty-ninth day of the disease. Note lesions on the upper lid, with a heart-shaped lesion at the external canthus. Treatment with potassium iodide had been started five days earlier, with an increase in the reaction. *C*, patient eleven days after iodide therapy had been started. Note beginning involution of the lesion. *D*, appearance approximately five weeks after beginning of iodide therapy. The lesions on the lid were markedly involuted. *E*, patient two months after iodide therapy had been started. The lesions no longer contained sporotricha and were almost flat.



Fig 2—Kodachrome showing appearance of the left upper lid, with typical lesions

sumption is that there were deeper nodes in the supraclavicular area, although these were not palpable. The patient also complained of headache. There was no rise in temperature.

Eleven days after iodide therapy was started there was pronounced improvement. All the lesions about the lid were smaller, as was the preauricular node. The postauricular node was slightly increased in size.

My colleagues and I next saw the patient six weeks after institution of the medication. She had discontinued taking the iodide one week previously because of its bad taste. We insisted that she resume taking the drug for at least another two weeks. The lesion on the lid was almost completely involuted. The one at the external canthus was still soft. A culture of material taken from it by aspiration was reported to show no growth.

The patient was last seen by us on Dec 7, 1945, at which time she showed a small healed scar on the left upper lid and one at the external canthus.

ETIOLOGIC FACTORS

Sporotrichosis is a mycosis caused by a parasite, the sporotrichum. Several members of the genus have been described, but it is generally agreed that *S. schenckii* is the only important member in this country as seen clinically. Many of the sporotricha occur as saprophytes and are found on vegetation in various parts of the world. They may also be found in the excreta of human and animal carriers. The fungus has been found in horses, dogs, rabbits, cats and rats. It has been discovered in the mouths and on the fur of healthy rats and on the coats of horses which had the disease. It is thought that the infection can occur as the result of rat bite.

The most common history is one of injury with a thorn, cactus or briar preceding the onset of the disease, and in many of the cases reported in the literature the patients have been florists⁵⁶ or people working around gardens. In 3 of the largest series reported, those from the South African mines, the occurrence was on the basis of rock and other mining injuries. In these series about 50 per cent of the primary lesions were at the site of injury. There have not been any cases reported in the literature of the disease being spread by contact between human beings. Moore and Manting⁵⁷ reported a case which was thought to be due to a mosquito bite, with lodging of the fungus in the skin at the site of the bite.

It is of interest that du Toit^{2b} successfully isolated a sporotrichum from dust floating about in the air and from timber during one of the South African epidemics. However, this author was not certain that the organism which he found was the one responsible for the disease.

⁵⁶ Gastineau, F. M., Spolyar, L. W., and Haynes, E. Sporotrichosis. Report of Six Cases Among Florists, *J. A. M. A.* **117**:1074 (Sept 27) 1941.

⁵⁷ Moore, M., and Manting, G. Sporotrichosis Following Mosquito Bite. *Arch. Dermat. & Syph.* **48**:525 (Nov) 1943.

among the workers, as it was less virulent when rats were inoculated and failed to produce clinical symptoms in human volunteers. This same author also stated that the "saprophytic existence of the fungus is known to reduce its virulence." Hence spontaneous reductions in the outbreaks tend to occur.

CLINICAL APPEARANCE

Clinically, sporotrichosis is seen as a chronic infection which is characterized by the formation of nodules in the lymph nodes, epidermis or subcutaneous tissues. These nodules tend to occur in chainlike formation and break down to form indolent ulcers. The initial lesion is commonly referred to as the chancre. While the infection is commonly found about the fingers, there have been reports in this country, prior to this paper, 7 cases of primary involvement of the eyes. The lesions of sporotrichosis are destructive, and, as has been pointed out earlier in this paper, fatalities have occurred.

About the eye, the disease most commonly manifests itself as ulcers of the lids and conjunctiva. These tend to begin as large subcutaneous gummas and break down to form ulcers. The latter are deep and may even develop in the bony walls of the orbit.

The globe itself can be implicated in three ways: by direct trauma, by direct extension or by the blood stream.

Lewis and Hopper⁵⁸ summarized the various clinical types as follows:

1. Localized lymphangitic type. Most of the South African and American cases fall under this head. Here, an initial lesion occurs on some exposed part of the body. This appears as a hard, round, movable and painless nodule, over which the skin can be moved. The nodule later becomes indurated and attached to the skin, which gradually changes in color from pink to purple and later becomes black and necrotic as the nodule softens and breaks down. While this lesion may, rarely, remain as the sole sign of the disease, it is not typical. Usually the initial lesion is followed in a week or more by a painless ascending inflammation in the regional lymphatics. In their course a chain of secondary subcutaneous nodules may be seen. The lymphatics do not typically become enlarged, as do the nodes in tularemia or in any of the disorders commonly included under the term Parinaud's conjunctivitis. Systemic symptoms and generalized involvement are uncommon, as is spontaneous recovery. The involuting lesions leave residual scars of varying degrees. The incubation period is about one week but may vary from three days to three weeks.

⁵⁸ Lewis, G. M., and Hopper, M. E. *An Introduction to Medical Mycology*, Chicago, The Year Book Publishers, Inc., 1939.

2 Disseminated subcutaneous type This form is more commonly described in cases from France and is not characteristically associated with an initial chancre Usually small, hard, painless nodules are found in the subcutaneous tissues Within a period of several weeks the overlying skin becomes involved, the nodules undergoing central softening and abscess formation The latter may leave indolent ulcers, with firm, indurated borders If untreated, new lesions continue to appear

3 Disseminated ulcerating type This type is much like the second form except for its tendency to earlier ulceration Du Toit stated that "many clinicians still tend to think only of the lymphangitic type, forgetting that the ulcerative and other forms are seen"

4 Epidermal type As I have previously stated, the initial lesion is usually subcutaneous In this type the epidermis at distant sites becomes secondarily involved Rare cases of pure epidermal disease have been described It is stated that the organism may remain as a saprophyte in the mouth or on the mucous surfaces after the disease is apparently cured, rendering the patient a possible carrier

5 Systemic type Here, the deeper tissues and viscera are implicated This is most commonly seen in cases of the disseminated type in which early treatment has not been given The skeletal system may be involved here, as may the inside of the globe

6 Allergic lesions Sporotrichids, similar to trichophytids, have been described by de Beurmann

Most American cases have been of the lymphatic type, whereas most of the French cases have been of the "multiple ulcerative type" The nodules and the granulomatous ulcers are apparently not necessarily directly connected, and either may appear on any part of the body Du Toit, however, stated that the lesions have never been reported on the feet or over the pelvic girdle

The ophthalmologist must bear in mind the fact that the lymphatic type is not the only one seen in this disease but that the ulcerative and other forms are commonly met with These tend to appear as small granulomatous ulcers, which are covered with a crust and beneath which an irregular base exudes serum and pus The pure pus is a dull yellow, but contamination with blood may give it a salmon pink appearance

Dangerfield and Gear¹ stated that in almost all their cases "the secondary lesions started within one or two weeks, along the course of the lymphatics" The earliest nodes become larger and softer If treatment has not been instituted, the overlying skin tends to become adherent and then to break down This results in the formation of a granulomatous ulcer akin to the primary lesions

PATHOLOGIC CHARACTERISTICS

The histologic picture is not diagnostic but is typical only of a granuloma. In Bedell's case the report of biopsy stated that "subacute and chronic inflammation" was present and that "lymphoma cannot be excluded." Du Toit stated that the essential pathologic feature is a reticuloendothelial response by the tissues, with the proliferation of these cells and the formation of nodules. Scattered among the reticuloendothelial cells are plasma cells, lymphocytes, occasional eosinophils and some multinucleated giant cells of the foreign body type. Characteristic follicles tend to be scattered throughout the lesion. These have a peripheral zone of reticuloendothelial cells with, in most cases, a central zone of neutrophilic polymorphonuclear cells. At the periphery of the nodule multinucleated giant cells are seen.

In Hill's case,⁴⁷ Verhoeff's report on the biopsy reads

[the] tissue contains large number of foreign body giant cells, but no tubercles resembling T B or syphilis. Some of the tissue shows considerable infiltration with lymphocytes and some only moderate infiltration with these cells. By ordinary methods of staining no organisms could be found in the tissues, but Verhoeff's modified gram stain shows filamentous organisms scattered through the tissues, some of great length. Some of these are surrounded by giant cells, others are not. The lymph gland shows the lymph sinuses distended with epithelioid cells.

IMMUNITY AND IMMUNE REACTIONS

Sporotrichosis has been reported among persons of practically all races. However, as I have previously stated, it is not very common in the tropics, nor has it been considered common among Negroes in Africa.

Moore and Manting⁵⁷ cited Fox and Lam, who in their wide experience among American Indians have never seen a case. Moore and Manting reported a case in a half-breed (French-Indian).

A positive reaction to the agglutination test may be demonstrated, but the value of this test has been nullified by the fact that the spores have been similarly agglutinated by the serum of normal controls. Bloch, cited by Lewis and Hopper,⁵⁸ expressed the belief that the intracutaneous test with an extract of *Sporotrichum* is valuable. This gave a positive reaction in our case. De Beurmann stated that a negative reaction rules out the diagnosis but that an occasional false positive reaction may occur. Du Toit stated the opinion that a positive cutaneous reaction is characteristically found in cases of the disease. In the experimental production of the disease in a volunteer, a positive cutaneous reaction occurred on the fifth day following inoculation.

Du Toit stated that the serum from patients with the disease agglutinated a suspension of the spores to a high titer (1:600) but that

the serum of some "normal" patients did almost the same. Therefore he felt that the complement fixation test was unreliable.

This same author found that the white rat was the most susceptible laboratory animal. When the males were given intraperitoneal inoculations, a typical scrotal reaction developed within ten days. The scrotum became swollen and inflamed and the testicles enlarged and fixed. Abscesses occurred in the peritoneum and the scrotum. When the animals were inoculated in the tail tip, the abscesses could be seen spreading up the tail.

DIFFERENTIAL DIAGNOSIS

Prior to the development of the chain of lesions there is nothing characteristic of the chancre which suggests sporotrichosis. When the chain of nodules or ulcers makes its appearance, sporotrichosis is suspected, although the other granulomas must be ruled out.

Syphilis and tuberculosis can be ruled out on the basis of the laboratory tests, the clinical pictures and the specific lesions seen at biopsy. Leprosy falls into somewhat the same category. When the conjunctiva is involved, it is often difficult to rule out Parinaud's conjunctivitis. Verhoeff reported the presence of *Leptothrix* in cases of this disease, and this organism has characteristics which differ from those of the sporotrichum. In cases of the oculoglandular type of tularemia the diagnosis may be confirmed by isolation of the organism from inoculated guinea pigs or by isolation of the specific agglutinins for *Pasteurella tularensis* in the patient's blood. When the conjunctiva is involved, trachoma must also be ruled out. Here, the typical conjunctival and corneal lesions, as well as the results of laboratory studies, are of aid.

The positive diagnosis of sporotrichosis rests on the identification of the organism. Direct smears of material taken by aspiration, preferably of an unopen nodule, may show the typical cigar-shaped organism as it appears in the tissues. However, most observers agree that direct smears are unsuccessful in too high a percentage of cases. Aspiration of the unopen nodule, followed by culture on Sabouraud's medium (or one of its modifications), will usually reveal the organism when examination is made with a hanging drop. The pus may be streaked on agar, but in our case this did not show any growth of the organism. On Sabouraud's medium the growth is usually recognizable in from three to five days. In early stages the colonies are small and white, with no aerial myceliums. As the growth increases, the surface of the colony becomes moist, wrinkled and membranous. The color may vary from cream to black.

Du Toit^{2b} stated that he kept the cultures at room temperature. The early colonies are white and star shaped.

These enlarge in a few days forming a colony of about one-half inch in diameter. The center of the colony is thrown into irregular folds, while smooth regular folds radiate down from the raised center to the smooth, flat periphery. After a few days a brownish-black pigment appears in the center of the colony. The appearance of these colonies is so characteristic as to allow diagnosis to the naked eye. George Lewis has confirmed this observation.

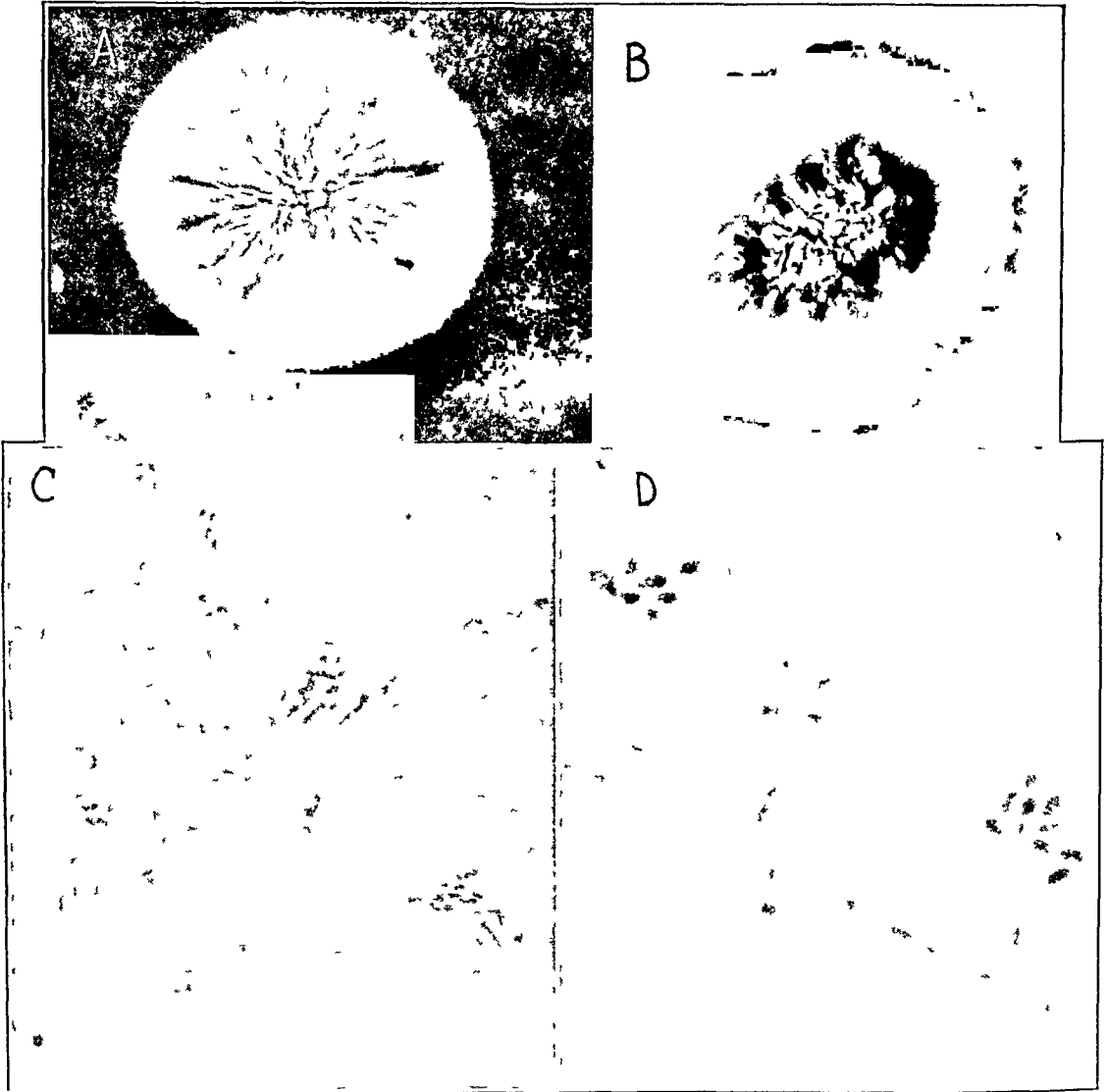


Fig 3—Two strains of *Sporotrichum schenckii*, showing a variation in the appearance of the colonies. *A*, stock strain after two weeks. *B*, primary culture after four weeks. *C*, culture mount showing clusters of spores and filaments ($\times 390$). *D*, culture mount showing clusters of spores borne at the tips of short stalks ($\times 715$). From Lewis and Hopper,⁵⁸ page 305.

Microscopically, the spores are seen to germinate in about twenty-four hours at one or both poles, sending out long filaments, which in a few days show much interlacing branching. The fungus appears as

delicate (2 microns in width), branching, septate hyphae, which bear conidia laterally or in groups on the ends of the lateral branches. The conidia appear in clusters of from 2 to 20 or as single spores. They are ovoid to spherical. In old cultures they are altered and appear as round, thick-walled structures, measuring from 2 by 4 to 2 by 6 microns.

If culture does not yield the organism, inoculation of laboratory animals may help, as I have pointed out earlier in this paper. Guinea pigs are usually immune, and white rats are best for inoculation.

PROGNOSIS

Most patients with sporotrichosis will respond well to treatment, even when seen with the disease in a fairly advanced state, provided that the deeper structures of the body are not yet involved. Implication of the globe (unless by direct perforation by the traumatizing and etiologic agent) is evidence of deep invasion and indicates that the organism has reached the blood stream. Numerous fatalities have been reported.

TREATMENT

Administration of potassium iodide is the treatment of choice. In all the reported American cases of ocular sporotrichosis the disease responded to this drug, with the exception of the cases of Hill and Sanford Gifford. Gifford advised administration of 4 drachms (15.5 Gm.) daily. The drug is usually given in the form of the saturated solution, the initial dose being 10 drops three to four times a day, and this amount is stepped up 5 drops per dose per day until the limit of tolerance has been reached. The treatment should then be continued at this level for several weeks and should not be stopped immediately with the appearance of a clinical cure. Most observers agree that the average period of medication is from one month to about six weeks. The iodides have no direct action on the sporotrichum. Davis expressed the belief that fibroblastic elements are stimulated and that through their proliferation and encapsulation a cure results. Iodides have been frequently used locally and by direct injection, in addition to their use orally. Roentgen therapy has also been used, but there is no evidence that it is of any great value in this disease.

Lewis⁵⁸ believed that surgical procedures are contraindicated, as they are of no benefit, except possibly for a single incision in the presence of fluctuation. He also suggested that wet dressings of solution of aluminum acetate N. F. (1:15) or of potassium permanganate (1:3,000) may be applied for a half-hour several times daily. Gentian violet medicinal in a 1 per cent aqueous solution may be used to irrigate the lesions, or strong solution of iodine U. S. P. in half strength

concentration may be applied. Lewis also suggested that thymol be tried with those patients who cannot tolerate iodides.

Noojin and Callaway⁵⁹ recently reported on the effectiveness of the sulfonamide compounds in vitro on *Sporotrichum schenckii*. They found sulfanilamide the most effective of the nine sulfonamide preparations which they used. They stated that it almost completely inhibited the growth of the fungus in vitro. It would seem, however, that the iodides should be given a fair trial in the treatment of sporotrichosis before other forms of therapy are resorted to.

SUMMARY

Forty-eight cases of ocular sporotrichosis have been reported in the world literature, including the case reported in this paper. Apparently in 34 of these cases the ocular disease was primary and in 15 secondary to involvement elsewhere in the body. In 2 of these cases (Nino and Sobly Bey⁶⁴) the diagnosis was in question.

The cases are distributed anatomically as follows: lids, 17, conjunctiva, 10, lacrimal sac, 2, conjunctiva and lacrimal apparatus, 1, brow, 1, intraocular, 5, orbit and lids, 5, cornea, 3, limbus, 1, uveal tract (without other lesions), 1, and lacrimal canal, 1.

Of the 48 reported cases, 10 have occurred in the United States and the majority of the remainder in France.

There are several excellent reviews of ocular sporotrichosis in the world literature. The first was that of Toulant,⁶⁰ who listed all the 23 cases occurring prior to 1913. Wilder and McCullough gave the first complete review in the American literature. This was followed almost immediately by Bedell's fine presentation. In 1922 Sanford Gifford again brought the literature up to date, with his first paper on the subject. Hill performed the same service in 1928. This is the last complete review of ocular sporotrichosis in the literature. It has been my attempt in this paper to bring the subject up to date again.

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59 Noojin, R. O., and Callaway, J. L. Effectiveness in Vitro of Sulfonamide Compounds on *Sporotrichum Schenckii*, *Arch Dermat & Syph* **49** 305 (May) 1944.

60 Toulant, P. *Essai sur la sporotrichose oculaire*, Thesis, Paris, 1912-1913, p. 390.

A POSITIVE CONTACT BALL AND RING IMPLANT FOR USE AFTER ENUCLEATION

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THIS IS a preliminary report on a new type of implant based on one year's use. This implant has a positive mechanical contact between the implant and the prosthesis, which provides a wide range and spontaneity of movement. The implant, in addition, eliminates sagging of the lower lid and minimizes sinking in of the upper lid.

Previously described implants, with the exception of the combined ✓ implant and prosthesis recently described by Ruedemann,¹ have been totally enclosed within Tenon's capsule and the conjunctiva or, in the case of evisceration, within the sclera and conjunctiva. In these circumstances, the available conjunctiva left to permit the prosthesis to rotate in the fornices has been diminished from that in the natural eye by the area occupied by the cornea. In the implant to be described, the anterior face is exposed, and thus the fornices have not been diminished. The exposed face, with an opening to receive a pin on the prosthesis, also permits mechanical contact and transmission of movement to the prosthesis.

Since the prosthesis does not rest on the lower lid at all, but is supported through its mechanical fitting to the implant, there is no sagging of the lower lid. Although it is not possible to be certain at the present time that sinking of the upper lid will not take place with this type of implant, it has not been sufficient in the patients so far operated on to require correction.

DESCRIPTION OF IMPLANT AND PROSTHESIS

Implant—The original design of the implant (fig 1) contemplated a plastic (methyl methacrylate) sphere 20 mm in diameter, narrowed anteriorly to permit the attachment of a metal ring approximately 19 mm in diameter, to which the four rectus muscles are attached. The ring is made of this size because this is the approximate diameter of the eye at the insertion of the rectus muscles. The anterior face of the implant is flattened and has a depression into which a gold pin is snugly, but not tightly, fitted. Originally these implants were made of three parts, put together by two screws at the operating table. However, it was not found practicable to do this, and Mr Cheetham, the dental technician at the

1 Ruedemann, A D. Read at the Eighty-First Annual Meeting of the American Ophthalmological Society, Nov 12, 1945.

Army hospital where this work was done, was able to make the implant in one piece. These implants required custom fitting of the pin when they were individually made. It is planned to make the entire implant of vitallium, so that the parts are interchangeable. The size of the ball is made 20 mm to allow the prosthesis to overlap when fitted and still not to be larger than the normal eye. The anteroposterior diameter is made 15 to 16 mm to allow space in front of the implant for the artificial eye. Later models of the implant have holes drilled in the ring to

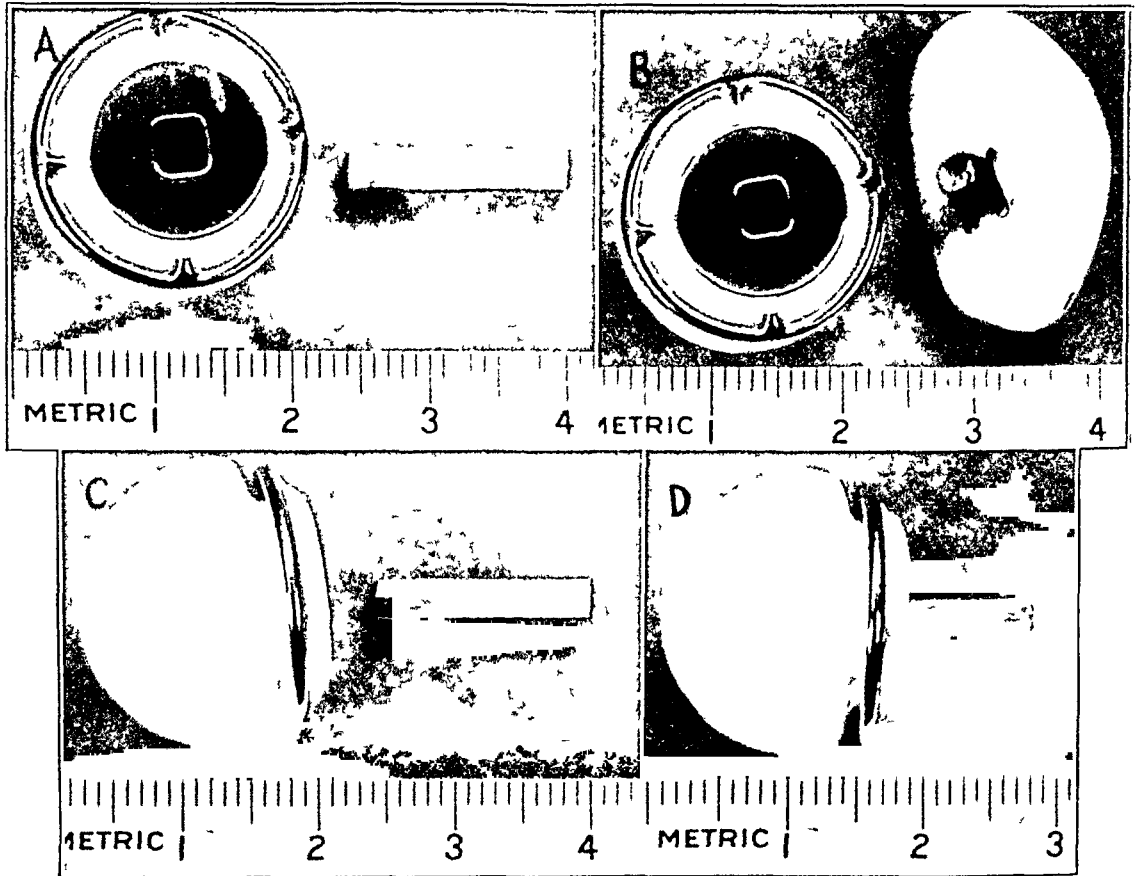


Fig 1—*A*, face view of implant, showing opening to receive the pin which is later attached to the prosthesis and the ring to which the rectus muscles are sutured, *B*, face view of implant and posterior view of prosthesis with pin attached, *C*, side view of implant and pin, *D*, side view of implant with pin in place

allow tissue to grow through and also slight projections on the inner aspect to hold the muscles in place during operation.

Small implants, 14 mm in diameter, with a 14 mm ring, were made to place in sockets from which a sphere had been removed. In this case the muscles were not isolated. It was found that the movement of the stump was totally transmitted to the prosthesis, but no more movement was developed than was present in the stump originally.

Prosthesis—The pin which is made with the implant is attached to a plastic artificial eye. It is necessary to center the pins carefully at the time of manufacture of the eye. The diameter of the eye has to conform as nearly as possible to the diameter of the other eye, otherwise the rotation of the eye would be unnatural in extreme positions, leaving a space either between the eye and the lids or between the eye and the socket. This is a decided departure from the normal procedure in making artificial eyes, in which the diameter is often made larger than the normal in order to obtain good contour of the lids. The eye is trimmed down until it is just large enough to stay inside the lids and show no edge on extreme movement to the right or left.

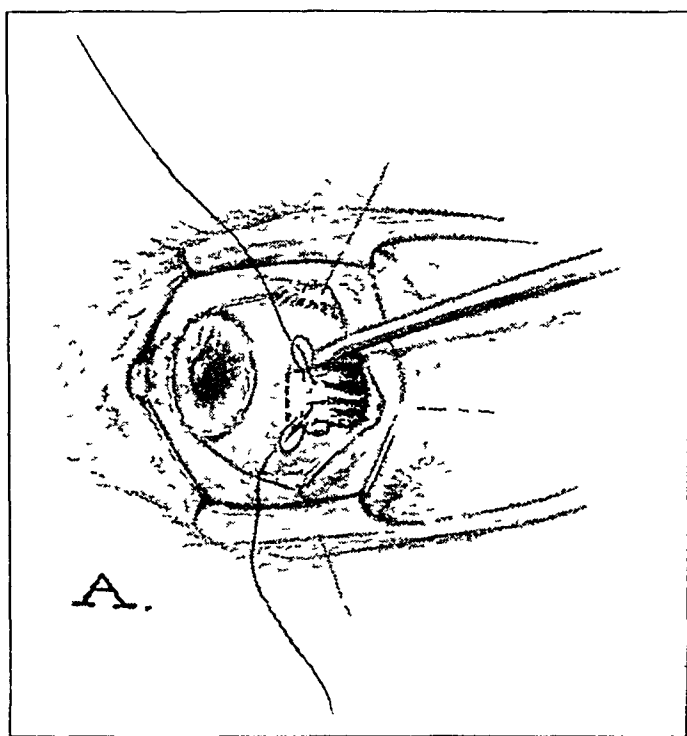


Fig. 2—Lateral rectus muscle isolated and 00 silk suture passed through tendon. A whip stitch is not necessary.

OPERATION

As with any enucleation, the procedure may be done with local anesthesia, using 2 per cent procaine hydrochloride and epinephrine for a retrobulbar injection, or with the patient under general anesthesia. In the latter case a retrobulbar injection reduces the amount of anesthetic used.

After routine preparation of the field, a Weeks speculum is inserted, and the conjunctiva is incised at the limbus with Stevens scissors and the dissection carried well back to the fornices. One of the rectus muscles is then picked up with a muscle hook and isolated, as in a muscle operation. A single-armed 00 black silk suture is passed through the

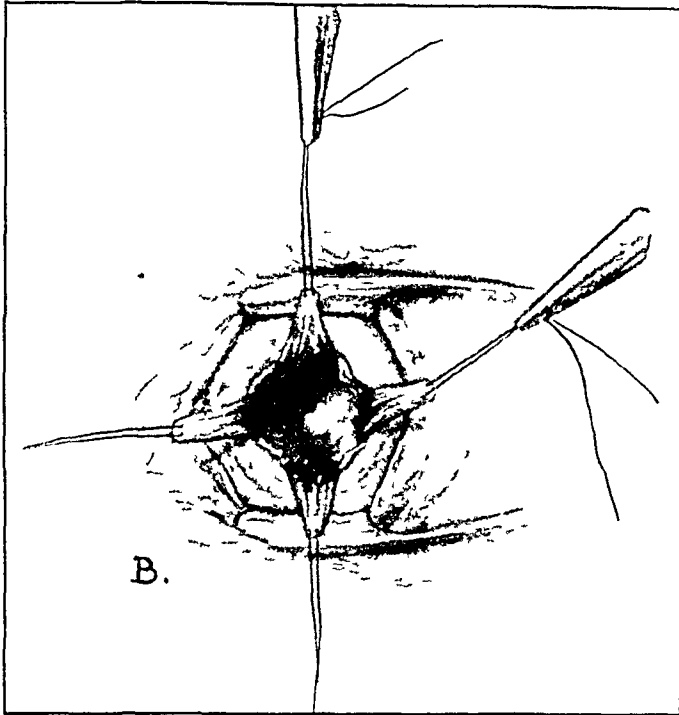


Fig 3—Enucleation complete

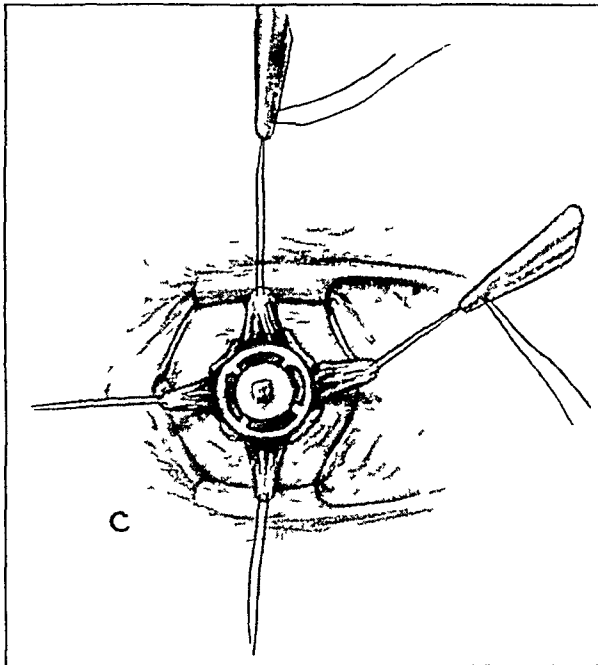


Fig 4—Ball and ring implant placed in Tenon's space

tendon and the muscle cut from its insertion (fig 2) This procedure is then repeated for the other three rectus muscles (fig 3) The enucleation is then completed in the usual manner and the eye delivered

Tenon's capsule is inspected by holding the margins forward with fine-toothed forceps, and the implant is then put into Tenon's space (fig 4) The assistant now holds the implant in place by grasping the pin with Kelly forceps The four silk muscle sutures are now passed through

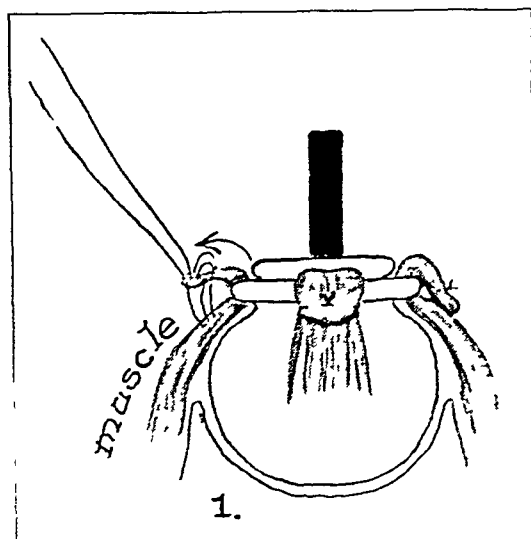


Fig 5—Drawing showing the manner in which the rectus muscles are carried through the ring and held in place with mattress sutures

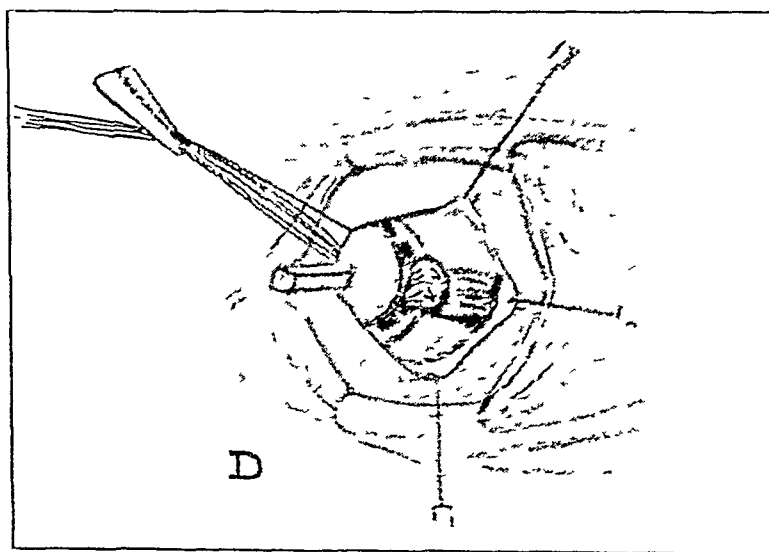


Fig 6—A rectus muscle sutured in place in the ring

the ring from below upward in their proper place The tendon of the inferior rectus muscle is grasped with von Graefe fixation forceps, and traction is made until approximately 4 mm of the muscle is through the ring Both needles, ($\frac{1}{2}$ inch [12 mm] curved) of a double-armed 000 black nylon mattress suture are passed through the muscle just below the ring, from below upward Both needles are then passed

through the tendon (fig 5) The fixation forceps are then given to the assistant, who holds the muscle downward so that the muscle is looped around the ring The suture is now triple-tied and cut (fig 6) The fixation forceps and the original black silk suture are removed This procedure results in the muscle being looped around the ring from below upward and tied on itself The three other rectus muscles are sutured in a similar manner (fig 7)

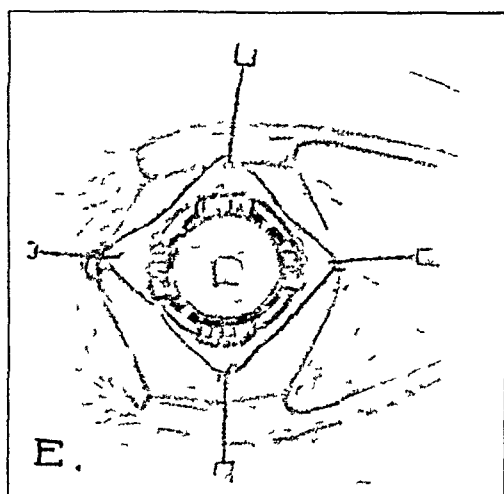


Fig 7—The four rectus muscles in place

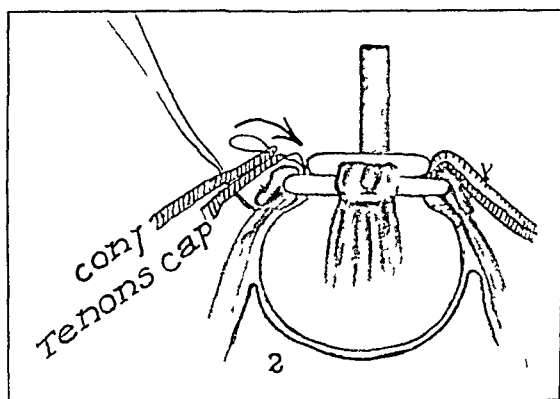


Fig 8—Drawing showing how the conjunctiva and Tenon's capsule are sutured around the ring, the sutures being passed in the reverse direction to those for the rectus muscles

Five to eight double-armed 000000 black silk sutures are now passed through the conjunctival edge from without inward and in the same direction through a firm part of the anterior edge of Tenon's capsule Both needles are then carried under the ring and out through Tenon's capsule and the conjunctiva (fig 8) When these sutures are pulled and tied, Tenon's capsule and the conjunctiva are rolled inward around

the ring on themselves. The central part of the implant remains exposed (fig 9).

The pin is now removed, and a small amount of petrolatum gauze is placed inside the lids and an adhesive dressing (Wheeler patch) applied

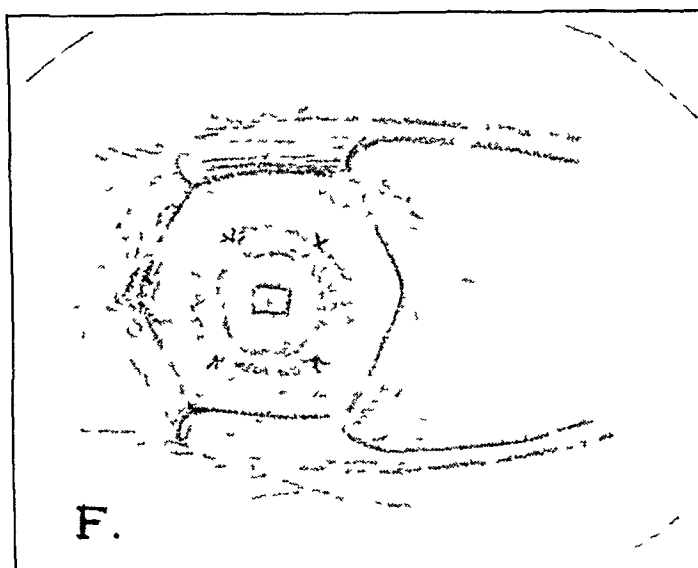


Fig 9—Completed operation. The anterior face of the implant is left exposed.

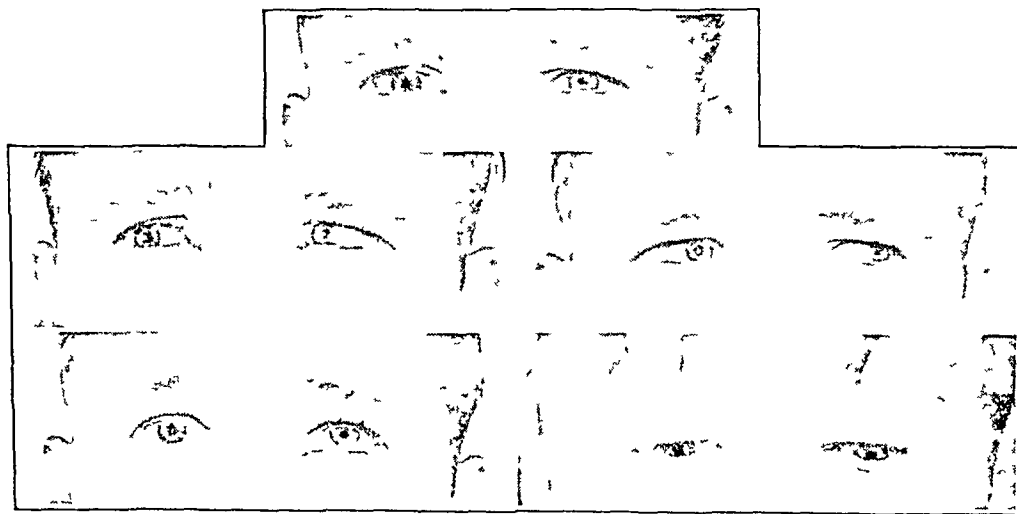


Fig 10—Photographs showing the extremes of movement, with prosthesis in the right socket.

POSTOPERATIVE CARE

The patient is allowed to be elevated or turned as desired and is allowed up as soon as he feels like it, usually in one or two days. The dressing is changed on the fifth and eighth days. No dressing is used after the eighth day. The conjunctiva-Tenon's capsule sutures are removed about the twelfth day, or whenever convenient. The patient is ready for fitting of the prosthesis in eighteen to twenty-one days.

COMPLICATIONS

In 3 cases implants were made in three parts—in all these the implant had to be removed. In 1 of the cases the patient had mild pneumonia and orbital cellulitis six months after operation, necessitating removal of the implant. No organisms were grown from his conjunctival sac. Two other implants had to be removed because the ring became exposed, owing, it was thought, to lack of firm suturing at the time of operation. Surgical gut was not found satisfactory for suturing the muscles. Incidentally, eight different ophthalmologists performed the operation during the developmental period.

It was not found practicable to resuture Tenon's capsule if the ring became exposed. Neither was it possible to use the implant in a case of scarring or other complications—the sutures would not hold.



Fig. 11—Photographs similar to those in figure 10, with prosthesis in the right socket.

If a muscle became exposed, it inevitably let go, allowing the implant to prolapse. Firm and properly placed sutures are very important. One smaller implant was placed in the sclera after evisceration but did not seem to give any better, if as good, results.

RESULTS

Twenty-two patients were operated on. Five implants were removed, for the reasons already stated. The amount of movement is indicated in the accompanying tabulation (figs. 10 and 11).

	Horizontal Movements	
Maximum	Minimum	Average
75°	65°	70°
	Vertical Movements	
Maximum	Minimum	Average
65°	65°	65°

SUMMARY

A new implant embodying a new direct method of transmission of movement is described. This implant gives to the prosthesis a larger range and greater spontaneity of movement than any previously used. The operative procedure, postoperative care and complications are discussed.

There are only two places in the body where a similar inert material projects to the exterior—the teeth and the nails. Time will tell whether these implants will be tolerated. This preliminary report is made one year from the date of the earliest retained implantation (August 1945).

Miss Helene Cleare made the illustrations, and Mr. A. Cheetham assisted in manufacture of the implants. Dr. Stanley Erpf and Dr. R. D. Stephens assisted in adapting the plastic prosthesis to this type of implant.

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Clinical Notes

AN AID IN FACILITATING POSTOPERATIVE DRESSING OF THE EYE IN PATIENTS WITH AKINESIS OF LIDS

WILLIAM D GILL, M D, SAN ANTONIO, TEXAS

SEVERAL years ago I called attention to a simple method of maintaining postoperative closure of the eyelids after akinesis of the orbicularis oculi muscle had been employed, which consisted in sealing the lashes of the upper lid to the lower lid by means of a small droplet of collodion¹. The method has worked satisfactorily over a period of years and is used routinely in my practice in all cases in which akinesis of the lids has been used. The possibility of an accident such as the patient's opening the eyelids beneath the dressing, with possible contact with the cornea, is prevented. With the collodion seal, the lids are maintained in approximation during the period that akinesis is in effect. The advantage over suture of the lids is evident. No additional wound is created, and the greater ease of use and the ease of removal, with absence of pain, will recommend its use. There is sufficient space on each side of the point of fixation of the eyelids with the collodion droplet to allow the introduction of medicaments, such as ointments, into the cul-de-sac and permit the escape of secretions from the eye. The chief objection to the use of this method has been the difficulty in opening the eye when the method had fulfilled its usefulness. At the time of the first postoperative dressing, when one desires to inspect the eye, it was formerly my custom to loosen the collodion fixation with a pair of finely pointed tissue forceps. This method is satisfactory but has certain objectionable features. More recently, in order to facilitate opening the lids and breaking the collodion seal, a short length of silk suture, 1½ to 3 inches (3.8 to 7.6 cm) in length, is introduced beneath the lashes after the eyelids have been closed and sealed with collodion. This can be accomplished before the sealing, but in such instances particular care has to be exercised to avoid incorporating the silk suture in the collodion droplet. When this silk suture is in position, its ends are brought together and draped onto the cheek below the eyelid, the two ends are tied together, and the customary dressing is applied. When the time comes to inspect the eye, it is a simple matter to grasp the ends of the silk suture and, with gentle traction, to separate the lids, as the suture will find its way between the lashes and the lower lid and the collodion seal will be easily and painlessly overcome. The small fragment of collodion usually remains adherent to a few of the lashes of the upper eyelid and can be pulled away with a small dressing forceps. The additional feature of using the silk thread to break the collodion seal has been most satisfactory, it has greatly facilitated the

¹ Gill, W D. A Way to Keep the Eyelids Closed After Infiltration Anaesthesia, *Ann Ophth* 58 269, 1928

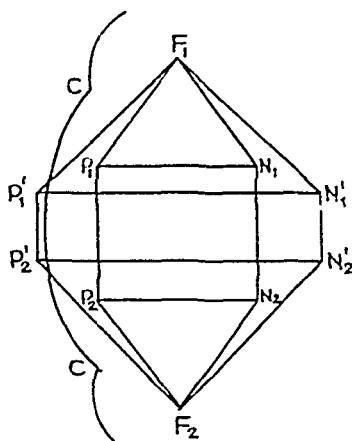
postoperative inspection of the eye and is considered less barbaric than the commonly employed lid suture and is worthy of more general use

323-325 Medical Arts Building

CARDINAL POINTS IN APHAKIA

JOSEPH I PASCAL, M D, NEW YORK

IN TWO previous communications¹ it was shown how the location and displacement of the cardinal points of the eye can be visualized and remembered by the use of the benzene ring. It was shown that when the eye accommodates the new position of the cardinal points can be represented by a long, slender ring situated inside the regular ring. When the crystalline lens is removed from the eye, the optical system of the eye is radically altered. Its refractive power has been decreased by about one fourth, and there has also been a shifting of the cardinal points. It can be shown similarly that the location and displacement of



Cardinal points in the normal and the aphakic eye

the cardinal points in the aphakic eye can be represented by a broad and flattened ring drawn from the regular ring representing the normal static eye

In the accompanying figure, the principal and nodal points of the aphakic eye are indicated by adding a prime to the corresponding letters P and N . It is seen that the focal lengths of the aphakic eye are longer, as shown by $P'_1 F_1$ and $P'_2 F_2$. This would be expected, since the eye is now a weaker refractive system. The two principal points P'_1 and P'_2 have moved forward from P_1 and P_2 toward the cornea and are closer together. In fact, they have moved forward so as to be a little in front of the cornea, as shown in the diagram. (They are also crossed, i e, P'_2 is in front of P'_1 —an interesting detail not shown.) The nodal points N'_1 and N'_2 have moved backward from N_1 and N_2 , away from

1 Pascal, J I. Cardinal Points in the Static and in the Dynamic Eye, *Arch Ophth* 34 319 (Oct) 1945, A Memory Scheme for the Cardinal Points, *ibid* 22 448 (Sept) 1939

the cornea, and are also nearer together. This produces less displacement of the axial rays.

The greater separation of $P' N'$ shows the longer effective "radius," which would replace the whole optical system of the aphakic eye. The backward movement of the nodal points shows that in the aphakic eye the retinal image is smaller than in the phakic eye. Of course, the retinal image is blurred, but disregarding the enlargement due to the diffusion circles and taking the image size only from the centers of the diffusion circles, one sees that the retinal image is smaller in the aphakic eye, since the nodal points are closer to the retina. The optical image, of course, is greatly enlarged.

37 West Ninety-Seventh Street

Obituaries

THEODORE LASATER TERRY, M D

1899-1946

Theodore Lasater Terry died suddenly of cardiac failure in Boston on Sept 28, 1946, in his forty-seventh year. Thus ended, all too early, a brilliant career in ophthalmology. Dr Terry was born in Ennis, Texas, Feb 19, 1899, the son of John S and Lucy Lasater Terry, the former a respected physician in his community.

He received his early schooling in Ennis, attended the Southern Methodist University and studied medicine at the University of Texas, from which he received his degree of Doctor of Medicine in 1922. After interning at the Henry Ford Hospital, in Detroit, he returned to the University of Texas to study general pathology, eventually becoming an associate professor in 1926. It was during this period that his interest in ophthalmology began, as indicated by the title of his first published paper in the *Texas State Medical Journal*, "Neurogenic Tumors of the Retina and the Optic Nerve". He completed the residency in ophthalmology at the Massachusetts Eye and Ear Infirmary in 1928 and was appointed assistant pathologist at that institution. Here he studied under Dr Frederick H Verhoeff, eventually becoming pathologist when Dr Verhoeff assumed the directorship of the Lucien Howe Laboratory of Ophthalmology in 1932. He also rose through the clinical grades at the Infirmary, becoming clinical assistant in 1929, assistant surgeon in 1932 and surgeon in 1939.

Dr Terry's accomplishments were so varied that in describing them it is difficult to know where to begin. He was an excellent clinician, surgeon and pathologist, but perhaps his greatest forte was teaching. Here he was completely at home, imparting to his students his own enthusiasm for the subject. He had strong convictions about the obligations of well trained ophthalmologists to give aid and counsel to the younger men. He was not one to be satisfied with a system of teaching just because it had always been in vogue, but was constantly trying new methods, most of which were thoroughly sound. At the time of his death he was assistant professor of ophthalmology at the Harvard Medical School, in charge of postgraduate teaching, and during the war had acted as head of the department, which he administered in excellent fashion in spite of many difficulties.

In the field of clinical research his name was well known, his chief studies dealing with keratoconus, malignant melanoma and ocular mal-

development in premature infants. Retrolental fibroplasia received the major part of his attention during the past few years. He devoted considerable time to clarifying this syndrome and bringing it to the attention of members of the medical profession as one of the leading causes



THEODORE LASATER TERRY, M.D.

1899-1946

of infant blindness in the country. In 1942 he received the certificate of merit from the American Academy of Ophthalmology and Otolaryngology for clinical research in this field. Just before his death, he had

planned an extensive research program in an effort to ascertain the cause of this malady among infants

Dr Terry was a faithful attendant at medical meetings, taking an active part in discussing papers of others, as well as contributing many of his own. He was the author of many scientific papers, covering a wide variety of subjects. A complete list is appended.

He was a member of the American Board of Ophthalmology, the American Ophthalmological Society, the American Academy of Ophthalmology and Otolaryngology, the American Medical Association, Section on Ophthalmology, the American College of Surgeons, the American Association for the Advancement of Science and the New England Ophthalmological Society, serving as past president of the last organization. He was also a trustee of the Association for Research of Ophthalmology, Inc., and president of the Foundation for Vision, which was formed this year to continue research on retrolental fibroplasia and other ophthalmologic problems.

There was another side to Dr Terry besides the scientific. His home and family meant everything to him. He was interested in photography, travel, current events, economics and politics, and in spite of the terrific demands his profession made on his time he did not fail to keep well informed about the outside world. He also felt strongly about doing his part in national defense, and not many of his colleagues were aware that he held a commission as lieutenant in the Medical Corps of the United States Naval Reserve until ill health forced his resignation, several years before the war. He had a keen sense of humor and was a delightful companion.

To his family and friends, to the institution he served and to ophthalmology in general, his loss is a tremendous blow.

EDWIN B. DUNPHY

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Correspondence

PERMEABILITY OF THE EXCISED CORNEA

To the Editor—Researches reported by DIS Holt and Cogan (The Cornea VIII Permeability of the Excised Cornea, as Determined by Measurements of Impedance, ARCH OPHTH 35:292 [March] 1946) have just come to our attention. The data in this paper, obtained through measurements of electrical impedance, definitely show that under the conditions used the corneal epithelium of excised beef corneas is virtually impermeable to various ions.

In an earlier paper in the same series (The Cornea II Transfer of Water and Sodium Chloride by Hydrostatic Pressure Through the Excised Cornea, ARCH OPHTH 27:696 [April] 1942) Cogan and Kinsey reported the results of osmotic studies concerning the semipermeability of the epithelium in excised cat corneas. In the latter paper, it was indicated in the authors' interpretation of the data that a difference in concentration of sodium chloride of approximately 0.03 per cent would be required to effect a transfer of fluid through the epithelium against a hydrostatic pressure of 400 mm of mercury, whereas the theoretic osmotic equivalent of this hydrostatic pressure was stated to be 0.007 per cent sodium chloride solution. If, as indicated, a difference in sodium chloride concentration of more than four times the theoretic would be required to effect a transfer of fluid under these conditions, we should interpret this to mean that the epithelium was possibly somewhat sievelike with respect to sodium and chloride ions and that a high degree of semipermeability was not indicated.

Actually, the theoretic osmotic equivalent of 400 mm of mercury is 0.07 per cent sodium chloride solution, not 0.007 per cent, as stated on page 703 of this paper. A reinterpretation of the data of Cogan and Kinsey based on this correction demonstrates almost as forcefully as the electrical impedance measurements in the recent study that the epithelium is virtually impermeable to sodium and chloride ions.

It is our interpretation that the curve in figure 5 of the paper by Cogan and Kinsey should be redrawn so that it passes through the zero line at a concentration difference of 0.07 per cent or greater, since it would be impossible to have an osmotic transfer of fluid below this concentration against a hydrostatic pressure of 400 mm of mercury. If the curve is to meet this requirement and at the same time fit the experimental data, it cannot be drawn as a straight line. (There is, indeed, no necessity for drawing the curve as a straight line, since the amount of water that passes through a biologic membrane is not necessarily directly proportional to differences in concentration, irrespective of whether it is perfectly semipermeable. Experimentally it is difficult to avoid the establishment of concentration gradients in this type of system.)

If the curve in the figure is redrawn so that it passes through the points for differences in sodium chloride concentration of 0.080, 0.150 and 0.250 per cent and at the same time conforms to the aforementioned considerations, it will be found that the curve intersects the zero line at approximately a 0.07 per cent difference in sodium chloride concentration, even when adequate allowance is made for the probable experimental errors.

The interpretation therefore indicates a virtually complete impermeability of the epithelium to these ions and more thoroughly justifies the conclusions of Cogan and Kinsey that "the corneal epithelium, for a biologic membrane, possesses a high degree of semipermeability with respect to sodium chloride solutions."

W O LUNDBERG, PH D , Austin, Minn
Hormel Institute, University of Minnesota

ALBERT L ANDERSON, Minneapolis
Precision Contacts

News and Notes

EDITED BY DR W L BENEDICT

GENERAL NEWS

Eye-Bank for Sight Restoration, Inc—The board of directors of the Eye-Bank for Sight Restoration, Inc, announce that Dr Herbert M Katzin, of New York, has been put in charge of the laboratory for ophthalmic research and that three fellowships have been granted for the purpose of studies of corneal vascularization, corneal pathology, vitreous replacement and vitreous transplant

Annual W. Thornwall Davis Postgraduate Course in Ophthalmology—The seventh annual W Thornwall Davis Postgraduate Course in Ophthalmology will be held from Jan 27 to Feb 8, 1947, at the George Washington University School of Medicine, 1335 H Street, N W, Washington, D C

During the first week there will be practical courses in ocular surgery, pathology and orthoptics During the second week lectures will be given by F Heed Adler, M D, J Mason Baird, M D, S Judd Beach, M D, Hermann Burian, M D, Ramon Castroviejo, M D, C Alvin Clapp, M D, F Bruce Fralick, M D, Deane B Judd, PH D, Peter C Kronfeld, M D, Walter I Lillie, M D, Philip I Salvatori, M D, Harold G Scheie, M D, Edmund B Spaeth, M D, and Frederick W Stocker, M D

For further information, apply to Ernest A W Sheppard, M D, professor of ophthalmology, executive officer, 1801 K Street, N W, District 4024, Washington, D C

Establishment of the Francis I Proctor Laboratory for Ophthalmologic Research.—A sum of over \$500,000 from the estate of Dr Proctor has been given to the University of California by Mrs Proctor for the establishment of the Francis I Proctor Laboratory for ophthalmologic research To assure adequate permanent space for the laboratory in the new science building which is to be constructed in the near future, Mrs Berthold Guggenheim has guaranteed a sum of \$65,000 toward the construction of this necessary space In the interim the laboratory is being housed in temporary quarters Dr Michael Hogan has been appointed director of the laboratory

SOCIETY NEWS

The Contact Lens Society.—The Contact Lens Society, purely scientific in object and organization, has been formed for the study of contact lens work in all its aspects Members may be medical or nonmedical The first scientific meeting will be held on Jan 20, 1947, at 5 30 p m, at the headquarters of the British Optical Association, 65 Brook Street, London, W 1

The officers of the society are as follows president, Prof Ida Mann, vice presidents, Mr F A Williamson-Noble and Mr K Clifford Hall, joint secretaries, Mr A G Cross and Mr G H Giles, treasurer, Mr C H Keeler Other members of the council are Messrs J H Doggart,

G B Ebbage and F A Juler, Sn Stewart Duke-Elder, and Messrs F Dickinson, H B Maillon G D McKellen and T Hamblin

The secretaries of the society, Mr A G Cross and Mr G H Giles, will be glad to supply information and forms of application for membership on receipt of a request addressed to 65 Brook Street, London, W 1

Washington, D C, Ophthalmological Society—The Washington, D C, Ophthalmological Society will hold a meeting on Monday, Feb 3, 1947, at 8 p m in the auditorium of the Medical Society of the District of Columbia, 1718 M Street, N Dr Peter C Kronfeld, Chicago, will speak on "Selected Cases of Retinal Detachment," and Dr F Bruce Fralick, Ann Arbor, Mich, on "The Problem of Thyrotropic Exophthalmos"

Ophthalmological Society of Egypt—The annual meeting of the Ophthalmological Society of Egypt will take place at the Memorial Ophthalmic Laboratory, Giza, Egypt, on Friday and Saturday, March 14 and 15, 1947, at 9 a m

Appointment of Medical Director of National Society for Prevention of Blindness, Inc—The National Society for the Prevention of Blindness, Inc, announces the appointment of Dr Franklin M Foote as medical director Dr Foote has been district health officer of the Kips Bay-Yorkville Health District of the Department of Health of New York City and, before that, chief of the Division of Local Health Administration, Connecticut State Department of Health He is assistant professor of public health and preventive medicine at Cornell University Medical College

Dr Foote is a native of Great Barrington, Mass, and received his degree of Doctor of Medicine from Yale University During World War II he served as major in the Medical Corps of the United States Army and was principally occupied in teaching preventive medicine at the Medical Field Service School, Carlisle Barracks, Pa, and at the Brook Army Medical Center, Fort Sam Houston, Texas

Centennial Meeting of the New York Academy of Medicine, Section of Ophthalmology—The centennial meeting of the New York Academy of Medicine, Section of Ophthalmology, will be held March 17, 1947, Dr Brittain F Payne, 17 East Seventy-Second Street, chairman

The subscription dinner (President's Gallery), at 6 15 p m, will be followed by a meeting of the executive session (Hosack Hall), at 8 15 p m

The papers of the evening are as follows "Past and Future Progress in American Ophthalmology," Dr Derrick Vail (by invitation), Chicago, "History of Ophthalmology in Canada," Dr John A Mac-Millan (by invitation), Montreal, Canada, "History of the American Board of Ophthalmology," Dr S Judd Beach (by invitation), Portland, Maine, "New York's Contribution in the Development of Ophthalmology in This Country," Dr Bernard Samuels, New York

Correspondence may be addressed to the secretary, Dr Milton L Berliner, 57 West Fifty-Seventh Street, New York

Ophthalmological Society of the United Kingdom—The annual congress of the Ophthalmological Society of the United Kingdom will

be held in Glasgow, Scotland, on March 27, 28 and 29, 1947. The president, Dr A J Ballantyne, will give an address entitled "De Senectute."

The subject for discussion will be "Rhino-logy in Relation to Ophthalmology," which will be opened by Dr John Marshall (ophthalmic surgeon), Mr Gilbert H Howells (otorhinolaryngologic surgeon), and Dr R McWhirter (radiologist).

On Friday afternoon there will be a clinical meeting at the Glasgow Eye Infirmary.

On Saturday afternoon visits have been arranged to the Corporation of Glasgow Art Galleries, Kelvingrove, under the guidance of the director, Dr T J Honeyman, and to the Hunterian Museum of the University of Glasgow, by invitation of the University Court.

The annual dinner of the society will be held on Thursday, March 27.

Honorary Secretaries are J H Doggart, 49 Wimpole Street, London, W (council business), E F King, 79 Harley Street, London, W (congress business).

UNIVERSITY NEWS

Graduate Training in Ophthalmology at the University of Toronto.

—The department of ophthalmology of the University of Toronto has undertaken postgraduate training during the past year. This has been aided by a generous annual grant from Mr Percy Hermant in establishing fellowships in ophthalmology. The postgraduate training for the fellows is now three years, of which the first is in the basic sciences of ophthalmology and the final two years are in clinical internships in one of the Toronto hospitals. Dr J R Gaby, of Toronto, and Dr A W Mahood, of Vancouver, British Columbia, Canada, have been appointed fellows for the current year. In addition to the fellowships, there are a number of clinical internships in ophthalmology of two years' duration.

The graduate instruction in ophthalmology in the hospitals in Toronto has been coordinated under the direction of the university. Didactic lectures are presented weekly to the interns by the members of the teaching staff in ophthalmology from October until May. On Saturday mornings ward rounds are made at the Toronto General Hospital and are attended by the interns in ophthalmology from the various hospitals.

The interns are rotated through the department of ophthalmology of the Hospital for Sick Children in order that they may become familiar with the medical and surgical procedures of children's ophthalmology.

The senior interns are given instruction in the preparation of scientific papers and their presentation, and each presents a paper at the Toronto Academy of Medicine, Section of Ophthalmology.

There have been a number of changes in the teaching staff of the department of ophthalmology of the university. Dr Walter W Wright has retired as professor of ophthalmology in the university and head of the department in the Toronto General Hospital and has been appointed professor emeritus. He has been succeeded by Dr A J Elliot. Dr A E MacDonald and Dr A Lloyd Morgan have been made assistant professors of ophthalmology, and the teaching staff of the department in the university has been increased by the appointments of Dr J S Crawford, Dr C E McCulloch, Dr J C Hill and Dr M E Albertson.

Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Biochemistry

DISTRIBUTION OF VITAMIN C IN THE LENS H E HENKES, *Ophthalmologica* 108: 11, 1944

Cylinders were cut from the lenses of a large number of species of animals, and the ascorbic acid content of the various layers was determined by the microtitration method of Glick and Biskind (*J Biol Chem* 110. 1, [June] 1935) The highest values were found in the subcapsular cortex, and the nucleus had the least The decrease in ascorbic acid content from capsule to nucleus differed in different species of animals The nucleus of cataractous lenses had a very low ascorbic acid content Guinea pigs with scurvy lost ascorbic acid in the cortex first, but this was quickly regained with appropriate feeding

F H ADLER

Conjunctiva

HEMORRHAGE FROM THE CONJUNCTIVA NOTES ON A CASE OF CAPILLARY ANGIOMA J P WHITE, *Brit J Ophth* 29 635 (Dec) 1945

A married woman aged 40, apparently healthy, had had bloody tears from the right eye on two occasions The bleeding was arrested by tightly applying a handkerchief to her eyelids The attacks were unrelated to menstruation

On eversion of the upper lid, a small reddish growth, about 3 by 2 mm, was noted on the palpebral conjunctiva near the superior margin of the tarsus The biomicroscope showed that it was highly vascular The growth, together with a piece of the tarsus, was excised In the tarsal region the epithelium was flat and thin In the area of the fornix the conjunctiva was laid in many folds and the epithelium was full of goblet cells One fold in particular contained many thin-walled vessels The reticulum was filled with lymphocytes

It would appear, therefore, that the capillary angioma was the source of the hemorrhage

The article is illustrated

W ZENTMAYER

Congenital Anomalies

OPERATION FOR CONGENITAL COLOBOMA OF THE UPPER LID R GAUFFRE, *Arch d'opht* 5 342, 1945

Congenital coloboma of the upper lid presents an immediate indication for operation, especially in order to protect the cornea The author describes the procedure which he used in the case of a child aged 4 years and in a second case, that of a child of 6 months A drawing illustrating the procedure accompanies the article He produces

akinesia in order to prevent voluntary closure of the lids, and this akinesia lasts ten days. He also uses a serum, which helps to avoid edema. These two procedures, he thinks, are contributory to the good results obtained.

S B MARLOW

Cornea and Sclera

SUPERFICIAL PIGMENTATION OF THE CORNEA R R BLONDIS, Am. J Ophth 29: 316 (March) 1946

Blondis reports 8 cases of pigmentation of the cornea. He states that the condition is not rare and believes it to be due to melanin which invades the cornea from the conjunctiva by way of the lymph spaces. Conclusive evidence of the character of the pigment is not yet available.

W S REESE

TRANSPLANTATION OF CORNEA O I SHERSHEVSKAYA, Am Rev. Soviet Med 2: 525 (Aug) 1945

Shershevskaya states that of the 435 keratoplasties performed in Filatov's clinic between 1922 and 1938 success was obtained in 24.1 per cent with the use of corneas from living donors. Filatov and his school developed the use of preserved cadaver corneas. In the Odessa clinic 264 transplantations were done in which this method was used. The successful results in this series amounted to 67 per cent. Filatov perfected the technic of the operation, suggested a series of new methods, constructed instruments which made the operation simpler and easier and widely popularized keratoplasty. His results have aroused the attention of ophthalmologists. Corneal transplantation is being performed in many hospitals throughout the Soviet Union.

J A M A (W ZENTMAYER)

A RARE FORM OF KERATITIS OF PROBABLE STREPTOCOCCIC ORIGIN P MATA LOPEZ, Arch Soc oftal hispano-am 4: 252 (April) 1945

In his many years of practice, the author has seen 3 cases which he has classified in the category designated by the title of this article. The condition is characterized by coordinated lesions of the skin and cornea in a fashion that he has never seen described before. The cutaneous lesion which initiated the condition in his 3 cases had been present for months before the onset. It is an eczematous dermatitis, proved to be of streptococcic origin, located in the retroauricular fold and giving slight symptoms. The corneal lesion then made its appearance, in the form of a superficial, infiltrated, ulcerative keratitis, unaccompanied with conjunctivitis due to any type of streptococcus. The patients, children, were otherwise healthy and gave a negative reaction to tuberculin. Streptococci could not be found in the corneal lesion, but the patients exhibited positive reactions to streptococcic allergens.

H F CARRASQUILLO

General

INFECTIONS OF THE EYES A SORSBY, Brit M J 1: 494 (April 7) 1945

At a meeting of the Fever Group of the Society of Medical Officers of Health, London, March 9, 1945, a discussion on the epidemiology and treatment of some ocular infections was opened by Sorsby.

He said that a provisional analysis of 9,622 certificates of blindness in the L C C and Middlesex areas had shown that 1,427 persons or 15 per cent were blinded by infectious diseases. In approximately three quarters of this 15 per cent ophthalmia neonatorum and syphilis were the responsible factors, ophthalmia neonatorum being the cause of blindness in 265, congenital syphilis in 516 and acquired syphilis in 290. In the remainder of the 15 per cent the factors contributing to blindness were largely trachoma (134 persons) and the various specific fevers (103 persons). The low incidence of infectious disease among the causes of blindness in England and Wales was in striking contrast to the conditions obtaining in countries like Egypt and in the Middle East generally, where over 80 per cent of all cases of blindness were due to the acute ophthalmias and, to lesser degree, to trachoma. At one time, however, infection was the major cause of blindness in England. At the beginning of the last century smallpox was the largest single factor, and toward the end of the century it was ophthalmia neonatorum. Even as late as 1922 ophthalmia neonatorum was the cause of blindness in some 30 per cent of all children at schools for the blind, by 1942 the incidence had fallen to about 10 per cent. This decline shifted the emphasis from infection to other factors—genetic anomalies in the young and degenerative lesions in the elderly.

Though the incidence of blindness from ophthalmia neonatorum has fallen so markedly, there is no evidence that the disease itself has declined to any extent. A clearer appreciation of the cause of ophthalmia neonatorum is needed, particularly as it has now been established that in only 20 to 25 per cent of cases is the disease of gonococcic origin. In at least 10 per cent of cases it is due to virus infection, and the etiology of this and of other types needs clearer recognition. While congenital syphilis has also declined to a gratifying extent, other transmitted maternal infections are only now being recognized, toxoplasmic choroidoretinitis being an example. The decline in the incidence of trachoma in childhood has only emphasized that there is still a considerable residue of trachoma in the adult population, and these persons constitute a possible source of epidemic outbreaks.

The sulfonamide compounds and penicillin are of great help in the treatment and elimination of infectious disease of the eyes. Ophthalmia neonatorum is now easily controlled by the oral administration of the sulfonamide drugs and the local application of penicillin. The acute ophthalmias of tropical and subtropical countries also respond well to the sulfonamide drugs, while in the treatment of trachoma local application of the latter had rendered the classic methods obsolete. These new drugs are, however, likely to be effective only in the bacterial infections of the outer eye. Intraocular inflammation is rarely bacterial in origin, and such common conditions as iritis and choroiditis still need intensive study.

ARNOLD KNAPP

EXPERIENCES WITH UNBREAKABLE CONTACT LENSES S. VON
GYORFFY, *Ophthalmologica* 108:44, 1944

One hundred patients wearing contact lenses made of an unbreakable artificial resin were observed over a period of five years. In 60 per cent of the cases the lenses were entirely satisfactory, in 20 per cent

they could be worn for a reasonable period, and in a remaining 20 per cent they could not be used. The author finds it impossible to foretell the patient's aptitude in the wearing of contact lenses and finds that the greatest difficulties are fogging, photophobia and the appearance of bubbles in the fluid

F H ADLER

General Diseases

OCULAR LEPROSY IN PANAMA R D HARLEY, *Am J Ophth* 29:295 (March) 1946

Harley studied 150 cases of leprosy in Panama and found ocular involvement in 90 per cent, 13 per cent of the patients being totally blind and 41 per cent having their vision reduced to 20/200 or less. The anterior segment is by far the more commonly involved. Therapy is palliative, and the leper withstands surgical procedures on the eyes better than one would suspect

W S REESE

OBSERVATIONS ON THE EFFECT OF RIBOFLAVIN ON THE ORAL LESION AND DYSPHAGIA, AND OF RIBOFLAVIN AND BREWERS' YEAST ON DARK ADAPTATION IN A CASE OF SO-CALLED PLUMMER-VINSON SYNDROME H POLLAK, *Brit J Ophth* 29:288 (June) 1945

An abstract of the author's summary follows

In a male patient admitted with a complete Plummer-Vinson syndrome (hypochromic anemia, due to iron deficiency) the angular stomatitis and dysphagia cleared up rapidly under treatment with riboflavin. A half year later, when the patient's blood picture was normal, severe impairment in dark adaptation was found. The course of dark adaptation was followed by serial tests with the Crookes instrument over a period of eight months. When the patient's performance had remained stationary for two months without treatment, a slight, but significant, improvement was recorded during treatment with riboflavin. After his dark adaptation had been allowed to fall back to the original level, the patient was treated with approximately 20 Gm of brewers' yeast daily for four months, during this period his dark adaptation gradually returned to normal, as shown by repeated tests.

A review is given of clinical evidence suggesting the association of a deficiency in riboflavin and allied factors of the vitamin B complex with the "iron deficiency syndrome," and the involvement of a "deficiency factor" in atrophic gastritis, which is considered an etiologic factor in the present case.

This hypothesis receives support from the present study, inasmuch as the impairment in dark adaptation together with the response to treatment with yeast may be taken as reflecting a disturbance in general metabolism, which appears reversible on administration of dietary factors of the vitamin B complex.

The observations recorded here and elsewhere suggest that dietary factors of the vitamin B complex may influence visual adaptation at low illumination under the experimental conditions herein described.

W ZENTMAYER

SOME OCULAR COMPLICATIONS OF SCRUB TYPHUS J MACASKILL,
Brit J Ophth 29: 537 (Oct) 1945

The causal organism in scrub typhus (tsutsugamushi fever) is the *Rickettsia nipponica*, which is believed to be transmitted to man by the larvae of a mite of the genus *Trombicula*. There is an incubation period of about twelve days. The site of entry may be marked by an eschar, and fever, severe toxemia, headache and prostration ensue. Diffuse glandular enlargement and a maculopapular rash are common. The mortality rate varies in different regions, ranging from 10 to 15 per cent. The essential pathologic feature is a generalized vasculitis affecting the arterioles and smaller vessels. This results in necrosis and destruction of the vessel walls, with extravasation of blood into surrounding tissues. Congestion of the conjunctiva occurs invariably in the acute phase of the disease. Subconjunctival hemorrhages (also seen in malaria), intense engorgement of the retinal veins, papilledema, retinal hemorrhages and bilateral optic nerve atrophy have all been met with.

A case is reported in which bilateral optic nerve atrophy occurred. For six weeks vision was reduced to hand movements, later visual acuity was 6/9 in each eye, and there was great depression of the periphery of the field. A toxic origin is considered as the probable cause of the optic nerve atrophy.

W ZENTMAYER

Glaucoma

CONGENITAL GLAUCOMA FOLLOWING MATERNAL RUBELLA DUP
GUERRY, Am J Ophth 29: 190 (Feb) 1946

Guerry refers to Gregg's paper on congenital cataract following rubella and reports 2 cases of congenital glaucoma in which the mothers had rubella in early pregnancy.

W S REESE

TANGENTIAL DISPLACEMENT OF THE IRIS IN CHRONIC GLAUCOMA
W J B RIDDELL, Brit J Ophth 30: 74 (Feb) 1946

Riddell calls attention to a condition present in the iris in certain cases of chronic glaucoma in which the normal radial arrangement of the iris stroma is replaced by a distribution running at a tangent to the pupillary margin. The change may involve a considerable segment or even the whole iris, and when it is well marked the pupil appears to have rotated around its own axis. Of 35 patients with chronic glaucoma the appearance was present in 14 (5 men and 9 women) and absent in 21 (12 men and 9 women). It is almost certainly a stage in the atrophy of the iris which occurs in the advanced phase of chronic glaucoma of long standing, but it can be found in the early stages of the disease. The author has observed the condition in a patient with megalocornea and cataract, but only when the pupil was dilated, and it appeared to be due to atrophy or rigidity in one small area at the pupillary margin.

The article is illustrated

W ZENTMAYER

Injuries

STEEL FOREIGN BODIES IN THE CILIARY BODY RECEIVED IN WAR INJURIES AND THEIR REMOVAL WITH ELECTROMAGNET N. IVANOV, *Vestnik oftal* 23:9, 1944

In an evacuation hospital, 347 extractions of intraocular foreign bodies with the electromagnet were performed during the years 1941 to 1943, the diascleral method being the one of choice. In 8 per cent, or 28 cases, the extraction of the foreign body from the ciliary body with the magnet was successful, and in only 2 cases was it not successful. The foreign bodies penetrated into the ciliary body through the cornea in 6 cases, through the limbus in 7 cases and through the sclera in 17 cases. The average size of the foreign body was about 3 mm, and they were mostly fragments of mines, grenades and bullets. In 15 cases the extraction was done within a month, in the others, within two to three months, after the injury.

Ivanov came to the following conclusions

- 1 Hemophthalmos is frequently observed in injuries of the ciliary body with steel fragments

- 2 Extraction of the foreign body should be done by the diascleral method after localization by the Comberg method and the electromagnet test

- 3 The incision of the sclera is made over the region of the ciliary body where the foreign body is located

- 4 There is little inflammatory reaction of the eye, despite the recent extraction with the magnet and a fresh injury to the eye

O SITCHEVSKA

MANAGEMENT OF INCREASED INTRAOCULAR PRESSURE FOLLOWING WAR INJURIES FIRST COMMUNICATION. C KALFA, *Vestnik oftal* 23:25, 1944

It is considered that the change in the vascular-nervous apparatus of the eye is the cause of increased tension after ocular injuries. In his previous work, Kalfa established the fact that there is increased tension after injury because of disturbance in the reflex which regulates the intraocular tension. At first active hyperemia, and then passive hyperemia arises because of the irritation of the autonomic apparatus of the eye which regulates the intraocular tension. If the autonomic system of the eye is eliminated by the local use of cocaine, there is no reactive hypertony. On this basis, in cases of contusion or injuries of the eye Kalfa applied a 3 per cent cocaine ointment or gave retrobulbar injections of procaine and epinephrine. This prophylactic therapy, he believes, frequently stopped or prevented the threatening symptoms of glaucoma complicating serious injuries of the eye. Case reports illustrate the author's point of view.

O SITCHEVSKA

Lens

A METHOD FOR THE EXTRACTION OF DISLOCATED LENSES FROM THE VITREOUS G BONACCOLTO, *Am J Ophth* 28:1335 (Dec) 1945.

Bonaccolto briefly discusses dislocation of the lens and suggests an operation which utilizes a conjunctival flap, sutures and peripheral

niidectomy The incision is made with a keratome and enlarged with scissoids, and the lens is removed with a loop He reports 7 cases

W S REESE

RUBELLA CATARACT CONGENITAL CATARACT AND OTHER DEFECTS FOLLOWING GERMAN MEASLES DURING PREGNANCY OF MOTHER A F M DEROETH and P B GREENE, Northwest Med 44 222 (June) 1945

DeRoetth and Greene report 2 cases of congenital cataract in infants In addition, one of the babies had microcephaly and microphthalmos, and the other had a congenital heart lesion The authors think that the cataracts should be extracted The Australian committee pointed out that avian and mammalian embryonic tissues are more susceptible to infection than the adult tissues This is the basis of Goodpasture's virus culture technic The human embryo possibly possesses the same susceptibility to infection The virus of rubella may pass the chorionic villi more readily than bacteria before a placental barrier has been developed The Australian committee made the following suggestions Expose all young girls to rubella, try to isolate the virus and prepare a vaccine against the disease, study the effect of convalescent serum, to be used on the pregnant mother in case she did not have rubella before The question arises whether therapeutic abortion is indicated if the disease is contracted in the first three months of pregnancy

J A M A (W ZENTMAYER)

METABOLISM OF THE CRYSTALLINE LENS M RIOS SASIAIN, Arch Soc oftal hispano-am 4•273 (April) 1945

After discussing thoroughly the metabolism of the lens, Sasiain reaches the following conclusions

The metabolism of the crystalline lens is performed through electronic changes in the presence of full anoxobiosis The presence of catalytic enzymes and oxyreducing systems are indispensable for the lenticular metabolism Transparency and the act of accommodation are the two factors for which the metabolism of the lens is important The reducing power of the lens must reach a certain level, which must be kept constant in order that transparency and accommodation be present When, owing to various causes, the metabolic harmony of the integrating elements of the crystalline lens is lost, there is precipitation of these elements, and opacification of the lens results

H F CARRASQUILLO

Methods of Examination

REPEATABILITY OF KERATOMETRIC READINGS R E BANNON and R WALSH, Am J Ophth 29 76 (Jan) 1946

Bannon and Walsh conclude that this study of the repeatability of keratometric readings on 100 eyes indicates that the keratometer is a reliable instrument and that the importance of the interpretation of individual examiners is negligible

W S REESE

STEREOSCOPIC OPHTHALMOSCOPY WITH FOCAL ILLUMINATION J
MALBRAN, Arch de oftal de Buenos Aires 19:455 (Nov) 1944

The author gives a brief historical review of all the methods of ophthalmoscopy and deals fully with the new method devised by Goldmann. In this method observation of the eyeground is made with the slit lamp of Haag and Streit and prisms which reduce to 5 degrees the angle formed by the luminous rays and the axis of the corneal microscope. It is also necessary to employ a contact lens which in certain respects differs from that devised by Koeppe. The advantages of the method are mentioned.

H F CARRASQUILLO

Neurology

UNILATERAL LACRIMATION ASSOCIATED WITH CHEWING. REPORT OF A
CASE. I B BENDER, Am J Orthodontics 31:692 (Nov) 1945

Bender reports a case in which stimulation of the area of the anterior palatine pad produced only congestion, lacrimation and pain. The effects were best produced by rubbing with a finger or by pressure of a denture during mastication. While the symptoms could be produced by reading small print and by blowing the nose, the dental factor was the more important. The pad area was definitely localized as the trigger point by the fact that unilateral biting and movements of the muscles of mastication did not reproduce the syndrome. When there is independent biting either on the right or on the left side, there is no compression or rubbing on the pad area. With normal chewing the force of mastication produces a pressure because of the closeness of adaptation of the dentures on the yielding mucosal tissues. The present case differs from those reported in the literature in that congestion and pain were associated with lacrimation. Whether this can be attributed to stimulation of both the autonomic and the sensory system is difficult to say.

J A M A (W ZENTMAYER)

DENIAL OF BLINDNESS BY PATIENTS WITH CEREBRAL DISEASE. F D
REDLICH and J F DORSEY, Arch Neurol & Psychiat 53:407
(June) 1945

Redlich and Dorsey observed 6 instances of denial of blindness over a period of eighteen months in a 600 bed hospital. Most examiners are reluctant to make any attempt to stress forcibly to the patient such a severe defect as blindness. All the patients who present such a syndrome are deteriorated and have disturbances of retention and orientation, hallucinations and delusions. The syndrome of denial of their own blindness in the authors' series was caused by a diabetic retinopathy in 1 patient, by atrophy of the optic nerve in another patient and by bilateral hemianopsia due to tumor or to vascular lesions in 4 patients. All these patients had diffuse cerebral lesions. All showed intellectual deterioration, disorientation, severe impairment of recent memory and retention, and confabulation. The existence of bilateral focal lesions of the visual radiations or of the occipital visual areas leading to bilateral hemianopsia seems to play an important part in the pathogenesis of the syndrome. The interruptions of reverberating circuits between the thalamus and the sensory cortex constitute the most prominent etiologic factor.

J A M A (W ZENTMAYER)

INDIRECT INJURY OF THE OPTIC CHIASMA A Case Report E. B. C. HUGHES, Brit J Ophth 29: 629 (Dec) 1945

A man aged 45 sustained a severe craniocerebral injury by striking the front of the head against a windshield. Examination one month later revealed no scalp wound, but there was severe bruising of both orbits and the frontal region. Roentgenograms showed a horizontal fissured fracture running above the frontal sinuses. On the right side this extended just over the midline and then ran vertically downward into the right frontal sinus, on the left side it ran as far laterally as the outer margin of the orbit and then extended vertically downward onto the roof of the orbit. There were complete bilateral anosmia, complete paralysis on the right side of the face with loss of taste and mild hemiparesis with increases of tone and of the tendon reflexes.

Both optic disks were abnormally pale, but the retinal vascular tree was normal. Visual acuity was 6/9 in each eye. The visual fields showed complete loss of the temporal field with involvement of fixation. The nasal fields were normal. Surgical exploration showed that the right optic nerve from the optic canal to its junction with the chiasm was normal. The left side of the chiasm and the left optic nerve were partially obscured by recent, grayish yellow, filmy adhesions, these were easily brushed away. The left optic nerve appeared normal. No gross injury of the chiasm could be seen. Four months later no changes had taken place in the optic nerves or the visual fields.

Hughes accepts the theory put forward by Traquair, Dott and Russell that the lesion is due to damage of the small vessels of the chiasm, most probably from a stretch injury.

The article is illustrated

W. ZENTMAYER

Operations

DACRYO-CYSTO-RHINOSTOMY T. K. LYLE, A. G. GROSS, J. F. SIMPSON and G. A. FRASER, Brit J Ophth 30: 102 (Feb) 1946

A description is given of a technic employed in dacryocystorhinostomy. The records of 56 cases in which the operation was performed are reproduced. The cases are analyzed to show the satisfactory results obtained with this procedure, even in cases in which previous surgical intervention has been carried out. The technic of the operation is shown by a number of adequate illustrations.

W. ZENTMAYER

USE OF CAUTERY IN PLASTIC OPERATION ON THE EYELIDS D. SIMPSON BRISTOL, Brit M J 2: 424 (Sept 29) 1945

The author used the electric cautery alone or in combination with the scalpel, though the major part of the work was done with the cautery. The conditions dealt with were ectropion, entropion, symblepharon, distichiasis and ptosis. The aim was to produce enough contracture by scarring of the underlying tissue to correct the deformity of the lids. The ordinary Weiss cautery was used, and the size of the point varied from 5 mm. to 1 cm. in length and 2 to 0.5 mm. in width at the base.

After anesthesia, entropion and ectropion were treated by introducing the red-hot point through the skin, or through the mucous membrane, down to the tarsal plate five or six times along the whole length of the lid. The point is held in each puncture about three seconds. If the condition is old and fairly prominent, it is necessary to excise a longitudinal strip of conjunctiva, of about one-third the width of the exposed conjunctiva. The treatment has to be thorough as an overeffect is not likely to follow.

Treatment of ectropion of the upper lid should be particularly thorough. The middle third of the conjunctiva is resected along the whole length of the lid, and then the red-hot point is plunged deep into the connective tissue, to and beyond the tarsal plate, at a number of places.

Symblepharon is a difficult condition. The author has attempted to disengage adhesions when the cornea was invaded. The cautery is applied to divide the adhesions at the most suitable spot, the point being carried down to the sclera. Each adhesion is treated in this way. The adhesions seldom reunite.

In treatment of distichiasis the point of the cautery is pushed down each hair follicle in turn and retained for two seconds. The lashes do not grow again, and no damage is done to the lid margins.

In cases of congenital ptosis in children the author has attempted to cause the levator muscle to form fresh adhesions to the tarsal plate. A row of six punctures is made just above the tarsal plate, and then each puncture is entered again, the point being passed upward and in the subcutaneous tissues as far as possible. The point should be 1.5 cm. long.

The author believes that this is a very useful procedure and that its simplicity is not generally recognized. In his own practice the results have been superior to those obtained with scalpel and stitch.

ARNOLD KNAPP

Orbit, Eyeball and Accessory Sinuses

OBSERVATION ON SO-CALLED THYROTROPIC EXOPHTHALMOS. H. ZONDEK and A. TICHO, *Brit. M. J.* 1: 836 (June 16) 1945.

Another form of exophthalmos than the one usually appearing with exophthalmic goiter has recently been described as attributable to the thyrotropic factor of the anterior lobe of the pituitary gland. This form goes under the name of thyrotropic exophthalmos.

In thyrotoxic exophthalmos the following factors are considered important from the etiologic point of view: (1) contraction of Muller's palpebral muscles, owing to increased sympathetic stimulation; (2) adynamia of the rectus muscles, which normally retract the eyeball; (3) occurrence of anatomic changes, which are generally not well marked. The extrabulbar muscles are of normal shape and consistency, though in some cases general wasting of the muscle fibers is present.

In thyrotropic exophthalmos the proptosis is more important in the development of the exophthalmos than is the widening of the palpebral fissure. The most important cause of the proptosis seems to be a muscular disorder, such as (1) diffuse extensive fibrosis, (2) edema, (3) abundant round cell infiltration or (4) a special type of degeneration.

resulting in fibrosis or absorption of muscle fibers (Molvany) In thyrotropic exophthalmos the proptosis is generally greater than in the thyrotoxic form and corresponds more closely to the malign form of the thyrotoxic variety

If the mechanical theory for the production of the exophthalmos does not hold true in all cases, its coincidence with diabetes insipidus, a symptom which is more or less characteristic of this disease, would indicate involvement of the pituitary gland or the diencephalic nuclei

The authors report on the examination in 3 cases of excessive exophthalmos which are recorded as instances of thyrotropic exophthalmos The ophthalmic manifestations were particularly severe in all these cases In 2 cases pronounced decalcification of the bones of the skull and enlargement of the sella turcica were present, this sign points to involvement of the pituitary-diencephalic region In both cases dextrose tolerance curves of diabetic type were obtained The abnormally high cholesterol level in the blood in 2 cases argues against hyperthyroidism In all 3 cases the disease responded favorably to diiodotyrosine In 1 case (postoperative exacerbation of the exophthalmos) administration of diiodotyrosine, in combination with irradiation of the pituitary body on two occasions, resulted in considerable improvement of the eyes (regression of proptosis and disappearance of chemosis and epiphora) and thus rendered surgical intervention unnecessary In view of the fact that the part played by the thyrotropic hormone in the production of this type of exophthalmos is doubtful, whereas the role of the pituitary-diencephalic system seems to be highly probable, the authors suggest the looser definition of "pituitary-diencephalic exophthalmos"

ARNOLD KNAPP

Parasites

OCULAR GNATHOSTOMIASIS K SEN, Brit J Ophth 29 618 (Dec) 1945

The gnathostoma was first recovered from the stomach nodule of a tiger by Owen, since then, it has been recovered from the stomach nodules of domestic cats, wild cats, leopards and dogs and from esophageal nodules in weasels in the Malay States, China, India and Japan The first case of human infection was reported by Levinson in 1890 The present case is probably the first reported instance of this worm in a human eye

A case of gnathostoma in the anterior chamber of the eye of a Hindu Brahmin aged 26 is described The onset was with a dull, aching pain on the left side of the nose, which extended to the left frontal and temporal regions, followed by swelling of the face, extending from the angle of the mouth to the roots of the hair These symptoms were followed by orbital cellulitis and vitreous and retinal hemorrhages There occurred two attacks of iritis with the development of gray nodules on the iris, which completely disappeared, leaving gray depressions on the iris Later, two more attacks of iritis occurred, with the formation of a single pigmented nodule on the iris in each attack The nodule completely disappeared, leaving no mark after the first attack

In the second attack, which was more severe, the pigmented nodule was seen to be the worm. The worm was removed at operation, and the eye made an uneventful recovery, though optic nerve atrophy developed.

It was not clear how the worm came to the side of the nose from the stomach without causing any signs or symptoms. The probable area of its entry into the eyeball from the orbit could be seen as a scar just below the macula.

The article is illustrated

W ZENTMAYER

Trachoma

ETIOLOGY OF TRACHOMA P DE GÓES, *Rev med brasil* 18:61, 1945

The author reviews the literature on the etiology of trachoma. He discusses the nosonomic concept of the disease and expresses the belief that it is a specific disease. The part played by constitution and other intrinsic causes which greatly influence the appearance and evolution of the disease are discussed. Various agents are considered as causative factors in the disease. Noguchi's work is studied in detail, the author believing that Noguchi's granulosis represents an incubated germ of the disease. He believes that the rickettsias described by Busacca represent elementary corpuscles of the virus of the disease. As to the Halberstaedter-Prowazek corpuscles, the author believes that they represent a special stage of the virus. The virus causation is discussed, this theory being, in the author's opinion, the most probable.

M E ALVARO

Toxic Amblyopia

QUININE AMBLYOPIA WITH SPONTANEOUS DETACHMENT J L HART, *Brit J Ophth* 29:375 (July) 1945

After the administration of quinine for a febrile condition the patient was delirious, with hallucinations, and claimed to be totally blind. The pupils were semidilated but reacted both directly and consensually. The eyes blinked when the hand was moved before the face. Care was taken to avoid an air-produced corneal reflex. In the right eye all but the temporal half of the disk was blurred. The vessels were scarcely visible at a distance from the disk. In the left eye the disk was pale. Eleven days after the onset the retina of the left eye was seen to be detached above the nerve head. On the twenty-first day vision in the right eye was limited to counting fingers at 2 meters and in the left eye to mere ability to count fingers. The patient received between 60 and 90 grains (0.39 to 0.585 Gm) of quinine.

W ZENTMAYER

Book Reviews

Augenärztliche Eingriffe Fifth edition By Professor J Meller and Dr J Bock, with additions by K Kofler and A Pillat Pp 460, with 267 illustrations Vienna Julius Springer, 1946

The fourth edition of this much enlarged and revised textbook appeared in 1938 and was reviewed in these ARCHIVES (21:561 [May] 1939). That edition was so popular that a new one soon became necessary and was ready in October 1944, but the terrible and tragic days which the war has brought to Austria, and particularly to Vienna, postponed its publication to this year. The excellent qualities of the fourth edition are just as outstanding in the fifth. The operations described are, with a few exceptions, those which have stood the test of time at the First Ophthalmic Clinic of the Allgemeines Krankenhaus in Vienna.

The young ophthalmic surgeon will not find the description of the fundamental principles in ophthalmic surgery so thoroughly treated and so well explained in any other book. In many cases only one method of operating is selected, as Meller says it is not the method itself but the experience with it which is the determining factor in success. When one method is not sufficient for all types of cases, such as those of glaucoma, a number of operations are described. The chapter on muscle surgery does not include the methods which are in general practice in this country. Corneal transplantation is not described and is apparently not practiced in the Vienna clinic. In the chapter on retinal detachment two additions are noted. The first is the return to Gonin's original method with the thermocautery when there is a vitreous pull from the radially placed operculum and when attempts with the high frequency current have failed to close a retinal hole. The second addition is the operation for shortening of the eyeball by scleral resection according to the method now practiced by Lindner. This method is suited for desperate cases of detachment in which no tear can be found, and especially in aphakic eyes or when other procedures have failed. A number of operations for glaucoma are described, but it is not clear which one the authors think the best in certain circumstances. The discussion of the intracapsular method of cataract extraction has been revised and has received a much more complete treatment at the hands of the co-editor, J Bock, and the various steps and the difficulties of the operation are fully outlined. At the same time, the book teaches that the beginner in ophthalmic surgery should first master the difficulties of the extracapsular technic and the intracapsular method should be selected for the cases in which this operation is superior.

Professor Meller closes his foreword with a dedication of farewell. Even if he withdraws from the active editorship of this book, future editions will carry his method of exposition of the principles of ophthalmic surgery and be of lasting value to every young ophthalmologist. An English translation, which is on the way, will be eagerly welcomed by many new readers.

ARNOLD KNAPP

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President Dr S Spence Meighan, 13 Woodside Pl, Glasgow, C 3
 Secretary Dr Alexander Garrow, 15 Woodside Pl, Glasgow, C 3
 Place Edinburgh and Glasgow, in rotation

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

Chairman Dr Jorge Malbrán, Buenos Aires
 Secretary Dr Benito Just Tiscornia, Santa Fe 1171, Buenos Aires

SOCIEDAD CUBANA DE OFTALMOLOGIA

President Prof Lorenzo Comas, Calle D #461, Vedado, Habana, Cuba
 Secretary Dr Oscar F Horstmann, Calle 5ta #702, Vedado, Habana, Cuba
 Time Second Tuesday of every month

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President Prof Dr Carlos Weskamp, Laprida 1159, Rosario
 Secretary Dr Arturo Etchemendigaray, Villa Constitución, Santa Fe
 Place Rosario Time Last Saturday of every month, April to November All
 correspondence should be addressed to the President

SOCIEDADE DE OPTALMOLOGIA DO NORTE

President Dr Alberto Cardenas

Secretary Dr Jorge Luis Castillo, Mendoza 421, Tucuman, Argentina

SOCIEDADE DE OPTALMOLOGIA DE MINAS GERAES

President Prof Hilton Rocha, Rua Rio de Janeiro 2251, Belo Horizonte, Minas Geraes, Brazil

Secretary Dr Ennio Coscarelli, Rua Aimores 1697, Belo Horizonte, Minas Geraes, Brazil

SOCIEDADE DE OPTALMOLOGIA E OTORRINO-LARINGOLOGIA DO RIO GRANDE DO SUL

President Dr Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul

Secretary Dr Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul

SOCIEDADE DE OPTALMOLOGIA E OTO-RHINO-LARINGOLOGIA DO BAHIA

President Dr Theonilo Amorim, Baria Avenida, Bahia, Brazil

Secretary Dr Adroaldo de Alencar, Brazil

All correspondence should be addressed to the President

SOCIETA OPTALMOLOGICA ITALIANA

President Prof Dott Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome

Secretary Prof Dott Epimaco Leonardi, Via del Gianicolo, 1, Rome

SOCIETE FRANÇAISE D'OPHTALMOLOGIE

Secretary Dr Rene Onfray, 6 Avenue de la Motte Picquet, Paris, 7^e

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

Secretary Dr K O Granstrom, Södermalmstorg 4, Stockholm, So

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President Dr D Arieh-Friedman, 96 Allenby St, Tel Aviv, Palestine

Secretary Dr Sadger Max, 9 Bialik St, Tel Aviv, Palestine

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman Dr Derrick Vail, 55 E Washington St, Chicago

Secretary Dr R J Masters, 23 E Ohio St, Indianapolis

Place Atlantic City Time June 9-13, 1947

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President Dr Alan C Woods, Johns Hopkins Hospital, Baltimore 5

President-Elect Dr C H McCaskey, 20 N Meridian St, Indianapolis, Ind

Executive Secretary-Treasurer Dr William L Benedict, 100-1st Ave Bldg, Rochester, Minn

Place Palmer House, Chicago Time Oct 12-17, 1947

AMERICAN OPHTHALMOLOGICAL SOCIETY

President Dr John W Burke, 1740 M St N W, Washington, D C

Secretary-Treasurer Dr Walter S Atkinson, 129 Clinton St, Watertown, N Y

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC

Chairman Dr Derrick Vail, 55 E Washington St, Chicago
 Secretary-Treasurer Dr Brittain F Payne, 17 E 72d St, New York
 Assistant Secretary-Treasurer Dr Hunter Romaine, 35 E 70th St, New York

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President Dr Alexander E MacDonald, 170 St George St, Toronto 5
 Secretary-Treasurer Dr L J Sebert, 170 St George St, Toronto 5

CANADIAN OPHTHALMOLOGICAL SOCIETY

President Dr J A MacMillan, 1410 Stanley St, Montreal
 Secretary-Treasurer Dr Kenneth B Johnston, Suite 1, 1509 Sherbrooke St W,
 Montreal

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President Mr Mason H Bigelow, 1790 Broadway, New York
 Secretary Miss Regina E Schneider, 1790 Broadway, New York
 Executive Director Mrs Eleanor Brown Merrill, 1790 Broadway, New York

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON
 EYE, EAR, NOSE AND THROAT

President Dr Anthony Ambrose, 31 Lincoln Park, Newark
 Secretary Dr William F Keim Jr, 15 Washington St, Newark 2
 Place 91 Lincoln Park South, Newark Time 8 45 p m, second Monday of
 each month, October to May

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Walter Stevenson, 510 Maine St, Quincy, Ill
 Secretary-Treasurer Dr William F Hubble, 866 Citizens Bldg, Decatur, Ill

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr P G Spelbring, 131 S Barstow St, Eau Claire
 Secretary Dr G L McCormick, 650 S Central Ave, Marshfield

HAWAII EYE, EAR, NOSE AND THROAT SOCIETY

President Dr F J Pinkerton, 7 Young Hotel Bldg, Honolulu
 Secretary-Treasurer Dr L Q Pang, 52 S Vineyard St, Honolulu 39
 Place Honolulu Time Third Thursday of each month

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President Dr Howard F Hill, 177 Main St, Waterville, Maine
 Secretary-Treasurer Dr Merrill J King, 264 Beacon St, Boston 16
 Place Massachusetts Eye and Ear Infirmary, 243 Charles St, Boston Time
 8 p m, third Tuesday of each month from November to April, inclusive

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President Dr D H O'Rourke, 1612 Tremont Pl, Denver
 Secretary-Treasurer Dr C Allen Dickey, 450 Sutter St, San Francisco

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Julius A Weber, 640 Stimson Bldg, Seattle 1, Wash
 Secretary-Treasurer Dr Barton E Peden, 301 Stimson Bldg, Seattle 1, Wash
 Place Seattle or Tacoma, Wash Time Third Tuesday of each month except
 June, July and August

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President Dr J Sheldon Clark, Sterling, Ill
 Secretary-Treasurer Dr Hairy R Warner, 321 W State St, Rockford, Ill
 Place Rockford, Ill, or Janesville or Beloit, Wis Time Third Tuesday of each month from October to April, inclusive

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr George Tiedke, 120 N Michigan Ave, Saginaw, Mich
 Secretary-Treasurer Dr James Curtis, 330 S Washington Ave, Saginaw, Mich
 Place Saginaw or Bay City, Mich Time Second Tuesday of each month, except July, August and September

SIOUX VALLEY EYE AND EAR ACADEMY

President Dr J C Decker, 515 Francis Bldg, Sioux City, Iowa
 Secretary-Treasurer Dr J E Dvorak, 408 Davidson Bldg, Sioux City, Iowa

SOUTHERN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr Savage Zerfoss, 165-8th Ave N, Nashville 3, Tenn
 Secretary Dr Alston Callahan, 908 S 20th St, Birmingham 5, Ala

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President Dr H L Brehmer, 221 W Central Ave, Albuquerque, N Mex
 Secretary Dr A E Cruthirds, 1011 Professional Bldg, Phoenix, Ariz

SOUTHWESTERN MICHIGAN TRILOGICAL SOCIETY

President Dr W M Dodge, 716 First National Bank Bldg, Battle Creek
 Secretary-Treasurer Dr Kenneth Lowe, 25 W Michigan Ave, Battle Creek
 Time Last Thursday of September, October, November, March, April and May

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr J V Foster, State College
 Secretary-Treasurer Dr J McClure Tyson, Deposit National Bank Bldg, Dubois

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President Dr E C Moulton, 619 Garrison Ave, Fort Smith
 Secretary Dr K W Cosgrove, 7 Urquhart Bldg, Little Rock

COLORADO OPHTHALMOLOGICAL SOCIETY

President Dr George H Stine, 23 E Pikes Peak Ave, Colorado Springs
 Secretary Dr J Leonard Swigert, 320 Republic Bldg, Denver
 Place University Club, Denver Time 7 30 p m, third Saturday of each month, October to May, inclusive

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President Dr Paul B MacCready, 442 Temple St, New Haven
 Secretary-Treasurer Dr W H Turnley, 1 Atlantic St, Stamford, Conn

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President Dr William O Martin Jr, Doctors Bldg, Atlanta
 Secretary-Treasurer Dr C K McLaughlin, 666 Cherry St, Macon

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr W E Stewart, 721 Wabash Ave, Terre Haute
 Secretary Dr Russell A Sage, 23 E Ohio St, Indianapolis
 Place French Lick Time First Wednesday in April

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr C S O'Brien, University Hospital, Iowa City
 Secretary-Treasurer Dr Carl A Noe, 120-3d Ave S E, Cedar Rapids

KANSAS STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY
 AND OTOLARYNGOLOGY

President Dr W B Gangei, Emporia
 Secretary Dr George F Gsell, 911 Beacon Bldg, Wichita 2

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr George S Adkins, 121 N President St, Jackson, Miss
 Secretary-Treasurer Dr Edley H Jones, 1301 Washington St, Vicksburg, Miss

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON
 EYE, EAR, NOSE AND THROAT DISEASES

Chairman Dr William T Hunt Jr, 1205 Spruce St, Philadelphia 7
 Secretary Dr Gabriel Tucker, 250 S 18th St, Philadelphia 3

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY
 AND OTOLARYNGOLOGY

Chairman Dr Edmond L Cooper, 1553 Woodward Ave, Detroit 26
 Secretary Dr Ralph H Gilbert, 110 Fulton St E, Grand Rapids

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Karl C Wold, 1051 Lowry Bldg, St Paul 2
 Secretary Dr William A Kennedy, 372 St Peter St, St Paul 2
 Time Second Friday of each month from October to May

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President Dr H Casebeer, 44 W Park Ave, Butte
 Secretary Dr Fritz D Huid, 309 Medical Arts Bldg, Great Falls

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha
 Secretary-Treasurer Dr John Peterson, 1307 N St, Lincoln

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY,
 OTOLOGY AND RHINOLARYNGOLOGY

Chairman Dr C W Buvinger, 50 Washington St, East Orange
 Secretary Dr Z Laurence Griesemer, 1145 E Jersey St, Elizabeth

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND
 THROAT SECTION

Chairman Dr Maxwell D Ryan, 660 Madison Ave, New York 21
 Secretary Dr Thomas H Johnson, 30 W 59th St, New York

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr A J Ellington, 412 S Spring St, Burlington
 Secretary Dr J A Harrill, Bowman Gray School of Medicine, Winston-Salem

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr E D Perim, 221-5th St, Bismarck

Secretary-Treasurer Dr M T Lampert, Minot

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Wilfred Belnap, 833 S W 11th Ave, Portland

Secretary-Treasurer Dr C W Kuhn, 1020 S W Taylor St, Portland 5

Place Good Samaritan Hospital, Portland Time Third Tuesday of each month

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Thomas F Furlong Jr, 36 Parking Plaza, Ardmore

Secretary Dr Benjamin F Souders, 143 N 6th St, Reading

Time Last week in April

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President Dr N Darrell Harvey, 112 Waterman St, Providence

Secretary-Treasurer Dr Linley C Happ, 124 Waterman St, Providence

Place Rhode Island Medical Society, Library, Providence Time 8 30 p m,
second Thursday in October, December, February and April

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Ruskin Anderson, 145 N Converse St, Spartanburg

Secretary-Treasurer Dr Roderick Macdonald, 330 E Main St, Rock Hill

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr George Burchfield Marville

Secretary-Treasurer Dr Sam H Sanders, 1089 Madison Ave, Memphis

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr F H Rosebrough, 603 Navarro St, San Antonio

Secretary Dr M K McCullough, 1717 Pacific Ave, Dallas

UTAH OPHTHALMOLOGICAL SOCIETY

President Dr E B Fairbanks, 315 Medical Arts Bldg, Salt Lake City

Secretary-Treasurer Dr Dean Spear, 516 Boston Bldg, Salt Lake City

Place University Club, Salt Lake City Time 7 00 p m, third Monday of
each month

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President Dr Thomas E Hughes, 1000 W Grace St, Richmond

Secretary-Treasurer Dr Francis H McGovern, 105 S Union St, Danville

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND
THROAT SECTION

President Dr George Traugh, 309 Cleveland Ave, Fairmont

Secretary Dr Welch England, 621½ Market St, Parkersburg

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr E L Mather, 39 S Main St, Akron, Ohio

Secretary-Treasurer Dr V C Malloy, 2d National Bank Bldg, Akron, Ohio

Time First Monday in January, March, May and November

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr B M Clme, 153 Peachtree St N E, Atlanta, Ga
 Secretary Dr Lester A Brown, 815 Doctors Bldg, Atlanta, Ga
 Place Academy of Medicine Time 7 30 p m, fourth Monday of each month
 from October to May

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman Dr Jonas Friedenwald, 1212 Eutaw Pl, Baltimore
 Secretary Dr Fred Reese, 330 N Charles St, Baltimore 1
 Place Medical and Chirurgical Faculty, 1211 Cathedral St Time 8 30 p m,
 fourth Thursday of each month from October to March

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President Each member, in alphabetical order
 Secretary Dr W Chunn Parsons, 425 Woodward Bldg, Birmingham, Ala
 Place Tutwiler Hotel Time 6 30 p m, second Tuesday of each month, Sep-
 tember to May, inclusive

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President Dr Benjamin C Rosenthal, 140 New York Ave, Brooklyn
 Secretary-Treasurer Dr Louis Freimark, 256 Rochester Ave, Brooklyn 13
 Place Kings County Medical Society Bldg, 1313 Bedford Ave Time Third
 Thursday in February, April, May, October and December

BUFFALO OPHTHALMOLOGIC CLUB

President Dr William M Howard, 389 Linwood Ave, Buffalo 9
 Secretary-Treasurer Dr Sheldon B Freeman, 196 Linwood Ave, Buffalo 9
 Time Second Thursday of each month from October to May

CENTRAL NEW YORK EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Uri Doolittle, University Bldg Syracuse
 Secretary-Treasurer Dr Alfred W Doust, 306 State Tower Bldg, Syracuse

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Each member, in alphabetical order
 Secretary Dr Douglas Chamberlain, Providence Bldg, Chattanooga, Tenn
 Place Mountain City Club Time Second Thursday of each month from
 September to May

CHICAGO OPHTHALMOLOGICAL SOCIETY

President Dr W A Mann, 30 N Michigan Ave, Chicago 2
 Secretary Dr J R Fitzgerald, 3215 W North Ave, Chicago
 Place Continental Hotel, 505 N Michigan Ave Time Third Monday of each
 month from October to May

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman Dr D T Vail, 441 Vine St, Cincinnati
 Secretary Dr A A Levin, 441 Vine St, Cincinnati
 Place Cincinnati General Hospital Time 7 45 p m, third Friday of each month
 except June, July and August

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman Dr M Paul Motto, Rose Bldg, Cleveland
 Secretary Dr H H Wygand, 624 Guardian Bldg, Cleveland
 Time Second Tuesday in October, December, February and April

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman Dr Burton Chance, 317 S 15th St, Philadelphia

Clerk Dr George F J Kelly, 37 S 20th St, Philadelphia

Time Third Thursday of every month from October to April, inclusive

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman Dr M Goldberg, 328 E State St, Columbus, Ohio

Secretary-Treasurer Dr W J Miller, 21 E State St, Columbus, Ohio

Place University Club Time 6 15 p m, first Monday of each month, from October to May, inclusive

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr L W O Jansen, 710 Medical Professional Bldg, Corpus Christi, Texas

Secretary Dr F B Kelly, 519 Medical Professional Bldg Corpus Christi, Texas

Time 6 30 p m, third Tuesday of each month from October to May

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Speight Jenkins, 1719 Pacific Ave, Dallas, Texas

Secretary Dr L Darrough, Dallas Medical and Surgical Clinics, Dallas, Texas

Place Dallas Athletic Club Time 6 30 p m, first Tuesday of each month from October to June The November, January and March meetings are devoted to clinical work

DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr H I McPherrin 406-6th Ave, Des Moines, Iowa

Secretary-Treasurer Dr C C Jones, Bankers Trust Bldg, Des Moines, Iowa

Time 7 45 p m, fourth Monday of every month from September to May

DETROIT OPHTHALMOLOGICAL CLUB

Chairman Members rotate alphabetically

Secretary Dr Wesley G Reid, 974 Fisher Bldg, Detroit 2

Place Club rooms of Wayne County Medical Society Time First Monday of each month, November to April, inclusive

DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Bruce Fialick, 201 S Main St, Ann Arbor, Mich

Secretary Dr William S Gonne, 619 David Whitney Bldg, Detroit 26

Place Club rooms of Wayne County Medical Society Time 6 30 p m, third Thursday of each month from November to April, inclusive

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President Dr Frank C Furlong, 713 Union St, Schenectady

Secretary-Treasurer Dr E Martin Freund, 762 Madison Ave, Albany

Time Third Wednesday in October, November, March, April, May and June

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr C R Lees, 602 W 10th St, Fort Worth 2, Texas

Secretary-Treasurer Dr Van D Rathgeber, 1305 Medical Arts Bldg, Fort Worth, Texas

Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except July and August

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND
OTO-LARYNGOLOGICAL SECTION

President Dr J Matt Robison, 1304 Walker Ave, Houston, Texas
Secretary Dr John H Barrett, 1304 Walker Ave, Houston, Texas
Place River Oaks Country Club Time 6 30 p m, second Thursday of each
month from October to June

INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr J Jerome Littell, 603 Hume Mansur Bldg, Indianapolis
Secretary Dr J Lawrence Sims, 23 E Ohio St, Indianapolis
Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each
month from November to May

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo
Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo
Time Third Thursday of each month from October to June The November
January and March meetings are devoted to clinical work

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Robert G Thornburgh, 117 E 8th St, Long Beach 2, Calif
Secretary-Treasurer Dr Kirt Parks, 605 Professional Bldg, Long Beach 2, Calif
Place Seaside Hospital Time Last Wednesday of each month from October to
May

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr William D Donohue, Los Angeles
Secretary-Treasurer Dr K C Brandenburg, 110 Pine Ave, Long Beach 2, Calif
Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time
6 00 p m, fourth Monday of each month from September to May, inclusive

LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky
Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky
Place Brown Hotel Time 6 30 p m, second Thursday of each month from
September to May, inclusive

LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Each member in alphabetical order
Secretary Dr James J Monohan, 31 S Jardin St, Shenandoah, Pa

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF
OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr P S Constantinople, 1835 I St N W, Washington
Secretary Dr Frazier Williams, 1801 I St N W, Washington
Place 1718 M St N W Time 8 p m, third Friday of each month from October
to April, inclusive

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Each member, in alphabetical order
Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn
Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m,
second Tuesday of each month from September to May

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Ralph T Rank, 238 W Wisconsin Ave, Milwaukee
Secretary-Treasurer Dr Frank G Treskow, 411 E Mason St, Milwaukee 2
Place University Club Time 6 30 p m, fourth Tuesday of each month from
October to May

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman Dr H V Dutrow, 1040 Fidelity Medical Bldg, Dayton, Ohio
 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio
 Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from
 October to June, inclusive

MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr L F Badeaux, 502 Cherrier St, Montreal, Canada
 Secretary Dr John V V Nicholls, 1414 Drummond St, Montreal, Canada
 Time Second Thursday of October, December, February and April

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr M M Cullom 700 Church St, Nashville, Tenn
 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville 3, Tenn
 Place James Robertson Hotel Time 6 30 p m, third Monday of each month
 from October to May

NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg, New Orleans
 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans
 Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday
 of each month from October to May

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman Dr Brittain F Payne, 17 E 72d St New York 21
 Secretary Dr Milton Berliner, 57 W 57th St, New York
 Time 8 30 p m, third Monday of every month from October to May, inclusive

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President Dr Benjamin Friedman, 6 W 77th St, New York
 Secretary Dr Benjamin Esterman 983 Park Ave, New York 28
 Place New York Academy of Medicine, 2 E 103d St Time 8 p m, first Monday
 of each month from October to May, inclusive

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr S R Shaver, 117 N Broadway, Oklahoma City
 Secretary Dr William Mussil, Medical Arts Bldg, Oklahoma City
 Place University Hospital Time Second Tuesday of each month from Sep-
 tember to May

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND
OTO-LARYNGOLOGICAL SOCIETY

President Dr A A Steinberg, 1502 Farnam St, Omaha
 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha 2
 Place Omaha Club, 20th and Douglas Sts, Omaha Time 6 p m dinner, 7 p m
 program, third Wednesday of each month from October to May

PASSAIC-BLUGEN OPHTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave, Paterson, N J
 Secretary-Treasurer Dr J Averbach, 435 Clifton Ave, Clifton, N J
 Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every
 month, except June, July and August

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President Dr L Waller Winckler, Philadelphia
 Secretary Dr Robert T M Donnelly, 255 S 17th St, Philadelphia
 Time First Thursday of each month from October to May

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr Jay G Linn, Jenkins Arcade, Pittsburgh
 Secretary Dr Robert J Billings, Jenkins Arcade, Pittsburgh
 Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each month, except June, July, August and September

READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Claude W Bankes, 212 N 6th St, Reading, Pa
 Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa
 Place Wyomissing Club Time 6 30 p m, third Wednesday of each month from September to July

RICHMOND EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Luther C Brawner, Professional Bldg, Richmond, Va
 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va
 Place Westmoreland Club Time 6 p m, second Monday of each month from October to May

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y
 Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPHTHALMIC SOCIETY

President Dr A Lange, 3903a Olive St, St Louis
 Secretary Dr William Kleinberg, Frisco Bldg, St Louis
 Place Oscar Johnson Institute Time Fourth Friday of each month from October to April, inclusive, except December, at 8 00 p m

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President Dr James P Aderhold, Medical Arts Bldg, San Antonio, Texas
 Secretary-Treasurer Dr Virgil S Steele, South Texas Bldg, San Antonio, Texas
 Place San Antonio Texas, and Brooke General Hospital Time 7 p m, second Tuesday of each month from September to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE,
 EAR, NOSE AND THROAT

Chairman Dr C B Cowan, 490 Post St, San Francisco
 Secretary Dr D Harrington, 384 Post St, San Francisco
 Place Society's Bldg, 2180 Washington St, San Francisco Time Fourth Tuesday of every month except June, July and December

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President Dr David C Swearingen, Slattery Bldg, Shreveport, La
 Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La
 Place Shreveport Charity Hospital Time 7 30 p m, first Monday of every month except July, August and September

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Robert L Pohl, W 1104, 21st Ave, Spokane, Wash
 Secretary Dr Malcolm N Wilmes, 407 Riverside Ave, Spokane, Wash
 Place Spokane Medical Library Time 8 p m, fourth Tuesday of each month except June, July and August

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President Dr A H Rubenstein, 713 E Genesee St, Syracuse, N Y
 Secretary-Treasurer Dr I H Blaisdell, 713 E Genesee St, Syracuse, N Y
 Place University Club Time First Tuesday of each month except June, July and August

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

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SURGICAL METHODS OF TREATING PARALYSIS OF THE SUPERIOR OBLIQUE MUSCLE

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PHILADELPHIA

ISOLATED paralysis of the superior oblique muscle is frequently encountered. According to Bielschowsky,¹ it is exceeded in occurrence only by paralysis of the external rectus muscle. Involvement of the superior rectus muscle is often encountered, but usually this is associated with paralysis of one or more of the other muscles supplied by the oculomotor nerve. While probably the most frequent, paralysis of the superior oblique is certainly the most puzzling single vertical paralysis with which the ophthalmologist has to deal. Congenital paralysis is not common, but bilateral involvement, usually thought to be congenital, is sometimes seen. The literature, however, records relatively few cases in which treatment has been carried out, and in these a great variety of surgical procedures have been offered. In fact, at some time or other almost every muscle attached to the globe has been used in one way or another. It is interesting to compare and analyze some of the methods employed.

PATHOPHYSIOLOGY

Before criticizing the various possible surgical procedures that have been proposed, it is well to have in mind the pathologic physiology of unilateral paralysis of the superior oblique muscle. This was discussed in detail in an earlier presentation.² The normal muscle has for its primary function the act of intortion, and for its secondary functions downward rotation and outward rotation (fig 1 A). From the position of "eyes front" the superior oblique intorts the corneal meridian and rotates the eye downward and outward. As the eye is rotated outward, the functions of intortion and outward rotation are increased, while the function of depression is decreased. On inward rotations (fig 1 B), the tortional and horizontal effects are minimized, while

From the Department of Ophthalmology, Graduate School of Medicine, University of Pennsylvania.

Read at a meeting of the College of Physicians of Philadelphia, Section on Ophthalmology, Oct 18, 1945.

1 Bielschowsky, A. Lectures on Motor Anomalies, Hanover, N H, Dartmouth College Publications, St Louis, Ophthalmic Publishing Company, 1940.

2 Krewson, W E, III. Comparison of the Oblique Extraocular Muscles, Arch Ophth 32 204 (Sept) 1944.

that of depression reaches its maximum. The superior oblique is synergistic with the contralateral inferior rectus, since the actions of the two muscles are similar for their respective eyes. The direct antagonist of the superior oblique is the homolateral inferior oblique.

With paralysis of the superior oblique the eye will be turned up and in and extorted (fig 2A),³ this is primary deviation, with the normal eye fixing. False projection will be down and out, the false

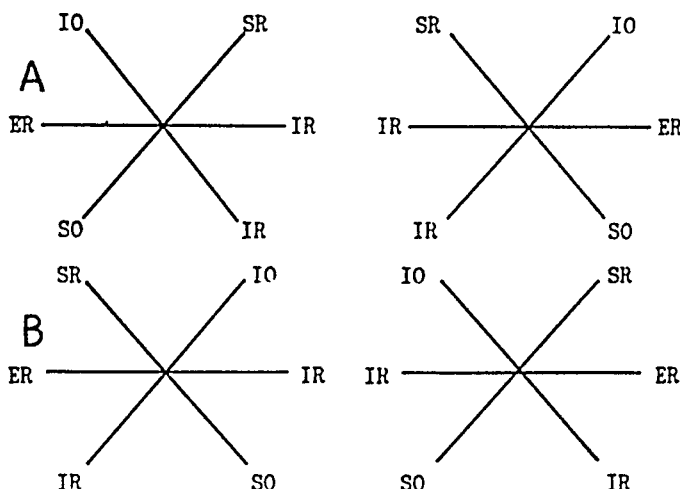


Fig 1—A, action of muscles from the primary position, B, muscles grouped as maximum elevators and depressors

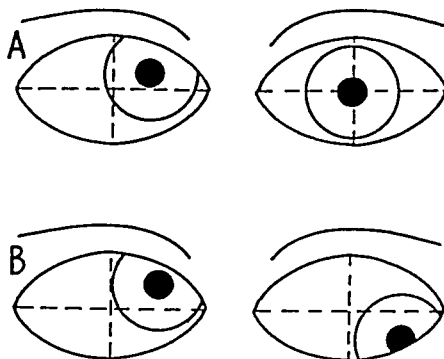


Fig 2—A, deviation up and in (primary deviation) and extorsion in paralysis of right superior oblique, B, limitation of downward rotation

image being tipped to the opposite side. The diplopia is annoying, but the torsional effects cause by far the more aggravating symptoms. The face is frequently turned down and to the opposite side, and the head may be tipped to the opposite shoulder. There is limitation of rotation downward, and this is most marked when looking down and in, where

3 In this paper, for purposes of comparison, all diagrams of eyes and muscle action are based on paralysis of the right superior oblique muscle, except those pertaining to bilateral involvement.

the muscle normally acts as a maximum depressor (fig 2 *B*). It is in this field, down and to the opposite side, that vertical diplopia is greatest. Since the paralytic eye is deviated inward, homonymous diplopia is encountered, although this may be nullified by a preexisting exophoria. In cases of long-standing paralysis secondary contracture of the direct antagonist, the homolateral inferior oblique, is sometimes found (fig. 3), this produces elevation of the paralytic eye on rotation to the opposite (normal) side.

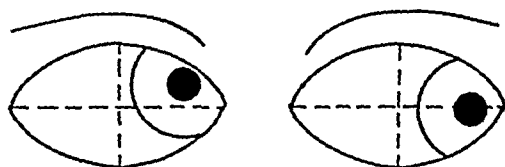


Fig 3—Elevation of paralytic eye on rotation to opposite (normal) side due to secondary contracture of homolateral inferior oblique

When the paralytic eye fixes, the normal eye is forced into secondary deviation by stimulation of the synergistic contralateral inferior rectus, causing the normal eye to turn down and in (fig 4 *A*). When the subject is looking downward, especially down and to the opposite (normal) side, overaction of the synergistic inferior rectus may be noted (fig 4 *B*). Some observers believe that there is an inhibitory palsy of the opposite (normal) superior rectus. Tilting of the head and

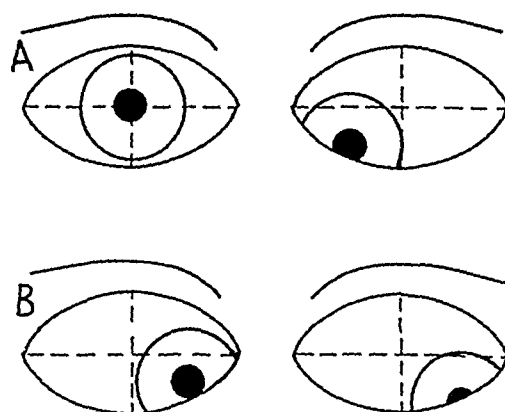


Fig 4—Paralytic (right) eye fixing. *A*, secondary deviation of normal (left) eye, *B*, overaction of synergistic, contralateral inferior rectus on looking down and to the normal side

turning of the face are modified by secondary contractures and choice of the fixing eye.

In cases of bilateral paralysis of the superior oblique the eyes are often found to be comitant, secondary deviation is not greater than primary deviation, and diplopia and torticollis are usually absent. The diagnosis is dependent on the finding of double hyperphoria (hyper-tropia), which is more marked on the right in the left lateral rotation and

more marked on the left in right lateral rotation. In each eye maximum limitation of rotation occurs on looking down and to the opposite side.

In consideration of the various methods of treatment, this review is limited to surgical procedures only, and the use of prisms, exercises and similar methods is not included.

TENOTOMY OF SUPERIOR RECTUS MUSCLE

Muller⁴ has described the operation of tenotomy of the homolateral superior rectus (fig 5 *A*) for relief of symptoms in paralysis of the superior oblique muscle. Although the procedure has been widely

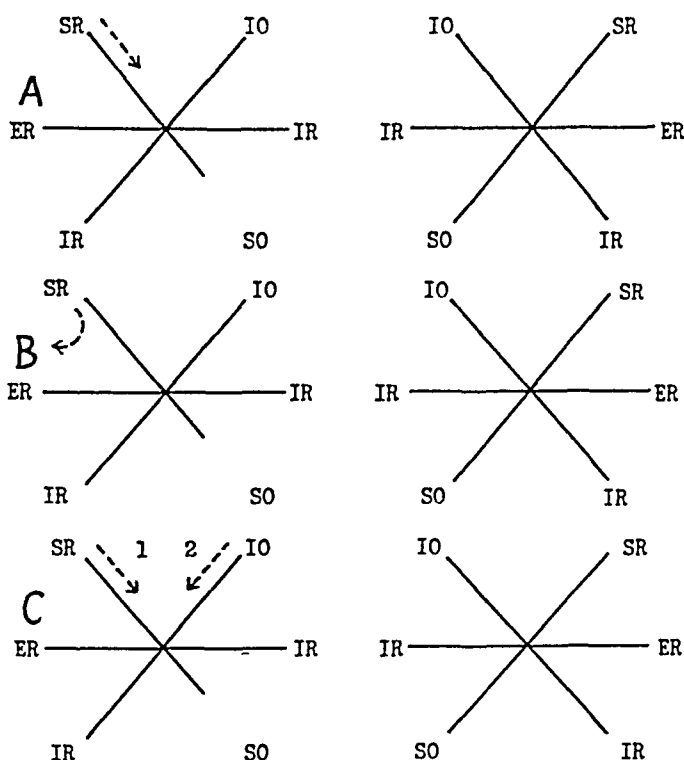


Fig 5—Tenotomy of homolateral superior rectus muscle. *A*, Muller's operation, *B*, Jackson's procedure, *C*, tenotomy of homolateral superior rectus and subsequent tenotomy of inferior oblique of same eye (Snell).

used, as Dunnington⁵ pointed out, it cannot succeed completely. The superior rectus aids the normal superior oblique in intortion, therefore tenotomy will increase the existing extorsion. Relief of the upward deviation will be partly accomplished, although the unopposed inferior oblique muscle, the remaining elevator, also will increase the extorsion. Jackson⁶ attempted to improve the operation by doing a partial tenotomy

⁴ Muller, L., cited by Dunnington⁵

⁵ Dunnington, J. H. Tenotomy on the Inferior Oblique, *Tr Am Ophth Soc* 27: 277, 1929.

of only the temporal fibers of the superior rectus. Later he⁷ moved the insertion backward and outward (fig 5 B), thus minimizing the elevating effect but at the same time increasing intortion, he reported 3 cases in which the paralysis improved with this method. Snell⁸ reported a case in which treatment with tenotomy of the homolateral superior rectus was unsuccessful and he had to resort to subsequent tenotomy of the inferior oblique of the same eye (fig 5 C). This procedure, of course, destroyed both elevators of the paralyzed eye, leaving the inferior rectus as the only vertically acting muscle.

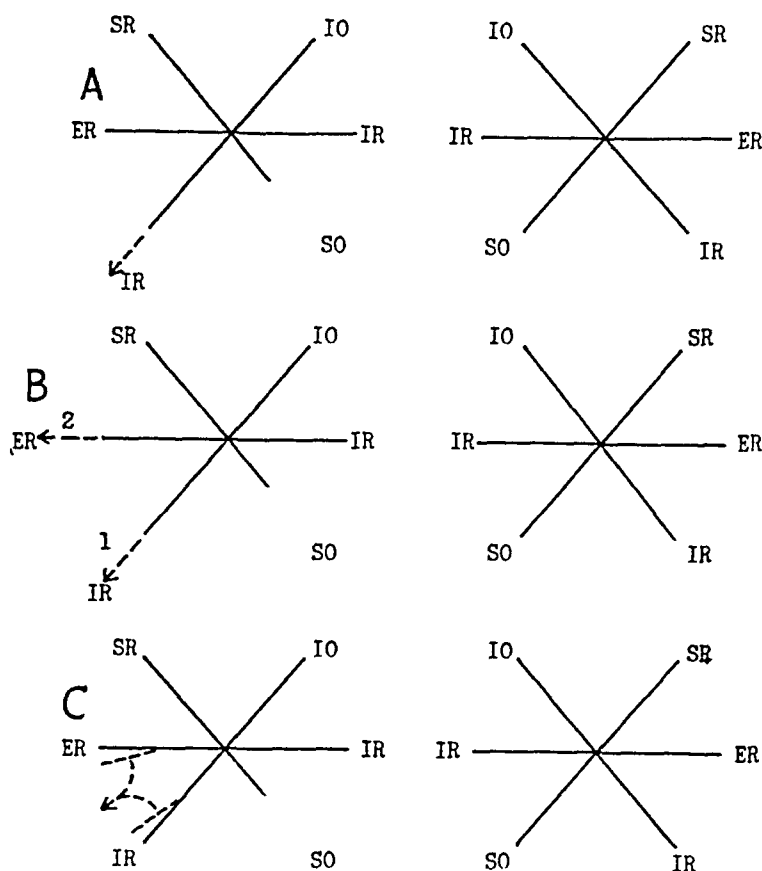


Fig 6—Advancement of homolateral inferior rectus muscle. A, Landolt's method, B, Bannister's modification of Landolt's method, C, Aurand's combined operation.

ADVANCEMENT OF INFERIOR RECTUS MUSCLE

Landolt⁹ advised and practiced advancement of the homolateral inferior rectus for relief of paralysis of the superior oblique (fig 6 A).

6 Jackson, E, in Wood, C A. American Encyclopedia of Ophthalmology, Chicago, Cleveland Press, 1917, vol 11, p 8238.

7 Jackson, E. Operation on the Tendon of the Superior Rectus Muscle for Paralysis of the Superior Oblique, Ophth Rev **22** 61, 1903.

8 Snell, A C. Injuries of the Superior Oblique Muscle. Report of a Case, Treatment, Arch Ophth **48** 111, 1919.

Strengthening of the one remaining depressor was to compensate for the shortcomings of the underacting muscle. This method was reported by others as being successful. Of course, increasing the downward rotation by strengthening the inferior rectus would not help much in cases of inward rotation in which vertical diplopia is greatest, and would tend only to increase the already existing extortion, and probably also inward rotation. Bannister¹⁰ in 1938, advised the use of this method and supplemented it by tucking or advancing the external rectus to overcome the homonymous diplopia due to inward rotation (fig 6 B). Aurand¹¹ combined the effects of the two procedures by transplanting the inferior half of the external rectus and the external half of the inferior rectus to a point near the temporal part of the limbus and between the insertion of the two muscles (fig 6 C). These operations cannot improve binocular vision down and to the opposite side, where it is needed most (figs 2 B and 4 B).

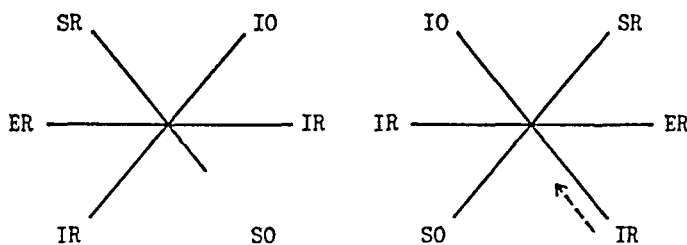


Fig 7—Wells's tenotomy of the contralateral inferior rectus muscle

TENOTOMY OF INFERIOR RECTUS OF OPPOSITE EYE

In 1860 Wells¹² stated that tenotomy of the contralateral inferior rectus "affords complete compensation for the paralysis" of a superior oblique muscle (fig 7). Von Graefe¹³ also advocated the method, but Landolt⁹ decried its use because of the limitation of downward gaze of the unparalyzed eye and the procedure was seldom used. Duane,¹⁴ however, revised the method in 1896, saying

"when a muscle is too weak, the effect upon the movement of the two eyes is the same as if the associated antagonist in the other eye is too strong,

9 Landolt, E. *Anomalies of Motor Apparatus*, in Norris, W. F., and Oliver, C. A. *System of Disease of the Eye*, Philadelphia, J. B. Lippincott Company, 1900, vol 4, p 69.

10 Bannister, J. M. *Surgical Suggestions as to Individual Paralysis of the Oblique Ocular Muscles*, *Am J Ophth* 2 537, 1928.

11 Aurand, cited by Wiener, M., and Alvis, B. Y. *Surgery of the Eye*, Philadelphia, W. B. Saunders Company, 1939, p 400.

12 Wells, cited by Dunnington⁵.

13 von Graefe, A., cited by Dunnington⁵.

14 Duane, A. *A New Classification of the Motor Anomalies of the Eye, Based upon Physiological Principles*, *Ann Ophth & Otol* 5 969, 1896.

and if we tenotomize this antagonist we shall limit the movement of the sound eye in the same sense and to the same extent as that in which the movement of the affected eye is already limited, i.e., both eyes will move again equally and with each other, although the movement of neither will be normal

Jameson,¹⁵ in 1922, introduced his recession operation, and Bannister,¹⁶ in 1925, presented his controlled tenotomy. Dunnington⁵ pointed out that some form of "recession of the contralateral inferior rectus is the operation most commonly employed in paralysis of the superior oblique"

TENOTOMY OF HOMOLATERAL INFERIOR OBLIQUE MUSCLE

In 1885 Landolt¹⁷ suggested tenotomizing the homolateral inferior oblique (fig 8*A*), and the operation has been reported by Duane,¹⁸ Posey,¹⁹ White,²⁰ Dunnington,⁵ Bielschowsky¹ and others. Snell⁸ used the operation, as noted previously. It is indicated in the presence of

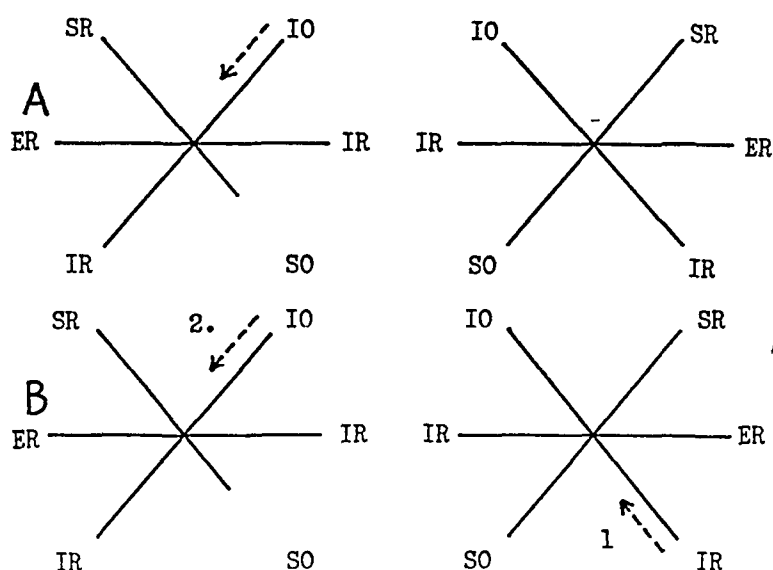


Fig 8—Tenotomy of homolateral inferior oblique. *A*, Landolt's procedure, *B*, combined recession of contralateral inferior rectus and subsequent tenotomy or recession of homolateral inferior oblique (Bielschowsky's procedure)

paralysis of the superior oblique when the direct antagonist, the homolateral inferior oblique, has undergone contracture and produces marked overaction, or upshooting, of the eye on inward rotation (fig 3)

15 Jameson, P. C. Correction of Squint by Muscle Recession with Scleral Suturing, *Arch Ophth* **51** 421, 1922

16 Bannister, J. M. Problems Connected with the Surgical Treatment of Ocular Palsies, *Tr Am Acad Ophth* **30** 160, 1925

17 Landolt, E., cited by Dunnington⁵

18 Duane, A. Isolated Paralysis of the Ocular Muscles, *Arch Ophth* **26** 317, 1897

19 Posey, W. C. Congenital Squint, *Tr Sect Ophth, A. M. A.*, 1907, p 253

20 White, J. W. A Review of Twenty-Seven Years with the Obliques, *Tr Pacific Coast Oto-Ophth Soc* **26** 112, 1941

Division of the muscle minimizes the vertical imbalance when the eye is turned toward the nose. The operation has undergone many refinements in technic of tenotomy at both the origin and the insertion. White²¹ and, after him Berens,²² Guibor²³ and others have devised methods for receding and transplanting the distal end of the muscle.

As pointed out by Bielschowsky,¹ in the majority of cases diplopia in the lower field is due to imbalance between the paralytic superior oblique and the homolateral, antagonistic and overacting inferior oblique (fig 3). Two operations are necessary, therefore, to permit binocular vision when the patient is looking straight ahead or to the opposite side, both above and below, namely, a recession of the contralateral inferior rectus and, later, a tenotomy or recession of the homolateral inferior oblique (fig 8B).

ELEVATION OF THE HYPOTROPIC EYE

When upshooting of the paralyzed eye occurs on looking to the opposite side, Spaeth²⁴ advocated elevation of the normal eye, which

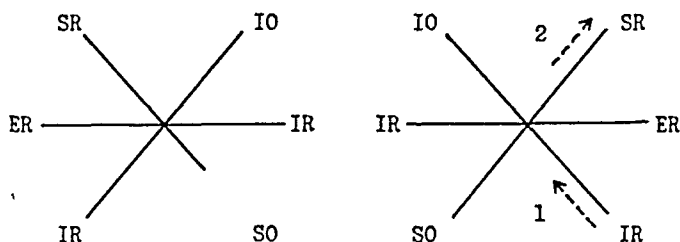


Fig 9—Recession of contralateral inferior rectus with advancement of contralateral superior rectus for elevation of hypotropic (normal) eye in upshooting of the paralyzed eye.

is in relative hypotropia. He suggested a wide recession of the contralateral inferior rectus followed or accompanied by an advancement of the contralateral superior rectus (fig 9). While this tends to weaken depression in the nonparalyzed eye, it preserves the action of the inferior oblique, which, although overacting, is the only vertically acting muscle effective in the paralyzed eye on inward rotation.

Moreover, he prefers to raise the normal eye to the level of the higher, or paralyzed, eye, since when the eyes are up the patient can read more comfortably by tipping the head forward with the chin in, if the para-

21 White, J. W. Surgery of the Inferior Oblique at or near the Insertion, *Tr Am Ophth Soc* 40:118, 1942.

22 Berens, C., in discussion on White²¹.

23 Guibor, G. P. Recession of Inferior Oblique Muscle from the External Rectus Approach, *Am J Ophth* 27:254, 1944.

24 Spaeth, E. B. Principles and Practice of Ophthalmic Surgery, ed 3, Philadelphia, Lea & Febiger, 1944, p 233.

lyzed eye is brought down, reading is less comfortable, since when the eyes are down the head must be tipped back with the chin out

ADVANCEMENT OF PARALYTIC SUPERIOR OBLIQUE MUSCLE

The superior oblique muscle with its reflected tendon is the most inaccessible of all the extraocular muscles because of its peculiar anatomic relations. However, advancement of its tendinous insertion has recently been perfected by Wheeler ²⁵ (fig 10) and is now used rather frequently

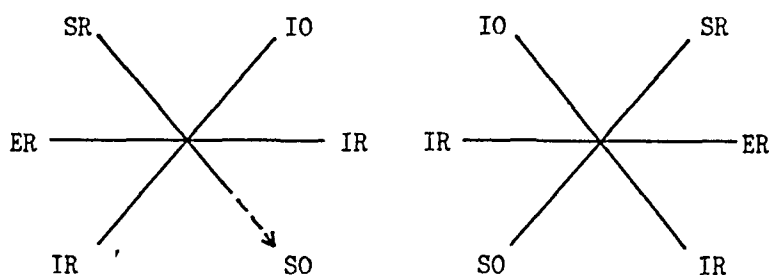


Fig 10—Wheeler's technic for advancement of a paralytic superior oblique muscle

by White ²⁶ and others, with good results. Peter ²⁷ suggested tucking the superior oblique. Shortening of this muscle not only tends to strengthen its weakened function but confines the operative procedure to the particular field or fields involved and does not permit disturbance in fields not primarily affected by the isolated paralysis.

COMBINED OPERATIONS

A combination of three of the aforementioned methods is frequently employed, the procedures being carried out in the following order, namely, recession of the contralateral, synergistic inferior rectus, tenotomy of the homolateral, antagonistic inferior oblique and shortening of the paralytic superior oblique (fig 11 A). This is the usual sequence followed by disciples of Duane, notably White ²¹ and Dunnington ²⁸. White ²⁰ wrote that if the vertical deviation is marked,

it may be safer to tuck the superior oblique first, this to be followed by a tenotomy of the inferior oblique of the same eye, a recession of the inferior rectus of the opposite eye, or both, depending on the subsequent measurements [fig 11 B].

This order is just the reverse of the preceding combination.

²⁵ Wheeler, J. M. Advancement of the Superior Oblique and Inferior Oblique Ocular Muscles, *Tr Am Ophth Soc* **32** 237, 1934.

²⁶ White, J. W. Personal communication to the author.

²⁷ Peter, L. C. *Extra-Ocular Muscles*, ed 3, Philadelphia, Lea & Febiger, 1941, p 354.

²⁸ Dunnington, J. H. *Surgical Treatment of Strabismus*, New York State J Med **38** 12, 1938.

By way of contrast, Gifford²⁹ weakened the homolateral inferior oblique if this was overacting, then did a recession of the opposite inferior rectus and, if the eye was still elevated, a recession of the homolateral superior rectus (fig 12 *A*)

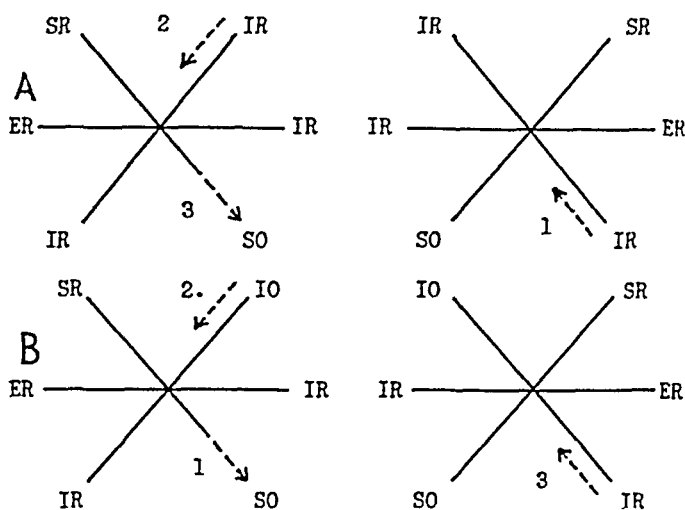


Fig 11—*A*, combined operation recession of contralateral inferior rectus, tenotomy of homolateral inferior oblique and shortening of paralytic superior oblique, *B*, White's modification of preceding combined operation

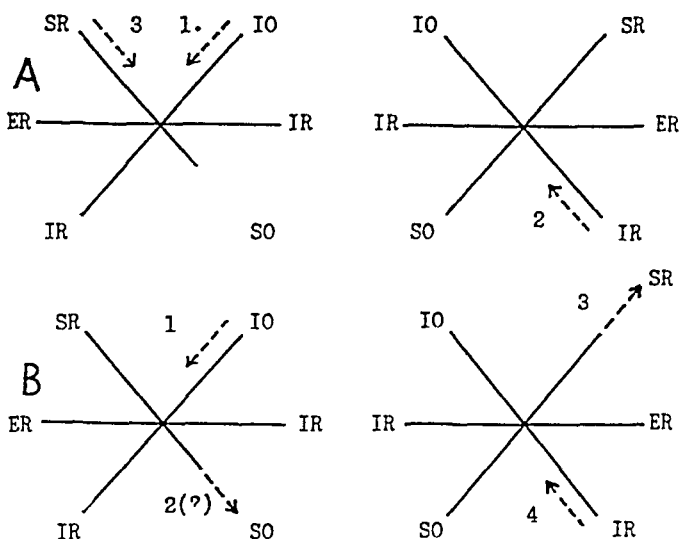


Fig 12—(*A*) Gifford's and (*B*) Worth's combined operation

Worth,³⁰ following orthopedic principles, advocated lengthening of the overacting, and possibly contracted antagonistic, homolateral inferior

29 Gifford, S R Results of Surgical Treatment of Paralysis of Superior Obliques and Superior Rectus Muscles, *Arch Ophth* 25 761 (May) 1941

30 Worth, C Worth's Squint or the Binocular Reflexes and the Treatment of Strabismus, ed 7, edited by F B Chavasse, Philadelphia, P Blakiston's Son & Co, 1938, p 532

oblique muscle Theoretically, this should be followed by a shortening of the weakened superior oblique, but he apparently felt that this was not feasible If necessary, the contralateral antagonist, the opposite superior rectus, is shortened, and, finally, recession of the contracted synergist, the opposite inferior rectus, is performed (fig 12 *B*)

BILATERAL PARALYSIS OF SUPERIOR OBLIQUE MUSCLE

In cases of bilateral paralysis of the superior oblique White ²⁶ varies his surgical procedure, depending on the patient's "choice of the fixating eye" If the patient fixes with the right eye on looking down and to the right (fig 13 *A*) and fixes with the left eye on looking down and to the left (fig 13 *B*), definite secondary contracture of the inferior oblique

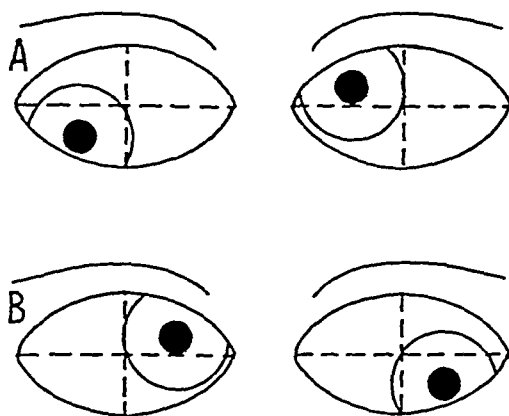


Fig 13—Bilateral paralysis of superior oblique muscle with secondary contracture of the inferior oblique muscle (*A*) when right eye fixes with patient looking down and to right and (*B*) when left eye fixes with patient looking down and to left

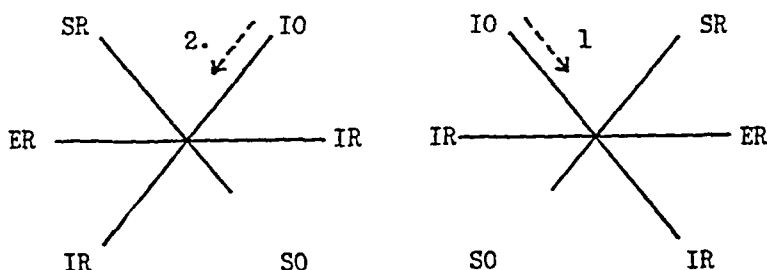


Fig 14—Bilateral tenotomy of inferior oblique muscle for bilateral paralysis of superior oblique muscle

muscle is usually found Bilateral tenotomy of the inferior oblique muscle is the preliminary procedure of choice (fig 14) On the other hand, if the left eye fixes on looking down and to the right (fig 15 *A*) and the right eye fixes on looking down and to the left (fig 15 *B*), secondary deviation is usually due to the action of the respective yoke muscles, the inferior rectus muscles In such cases a recession or tenotomy of each inferior rectus is indicated (fig 16)

When both superior oblique muscles are paralyzed, the respective contralateral inferior rectus in each eye should be weakened, theoretically,

for the reasons previously mentioned. However, as Spaeth²⁴ pointed out, this would produce the complete loss of both depressors of each eye. Instead of this radical procedure, Jaensch³¹ has recommended the con-

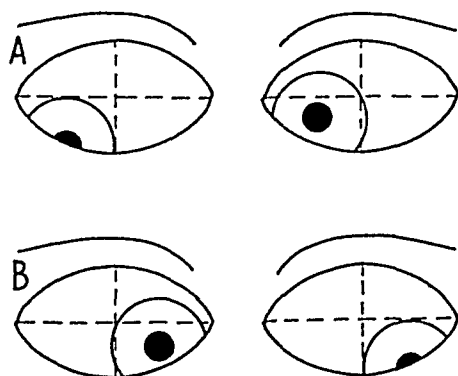


Fig 15—Secondary contracture of inferior rectus complicating bilateral paralysis of superior oblique (*A*) when left eye fixes on looking down and to right and (*B*) when right eye fixes on looking down and to left

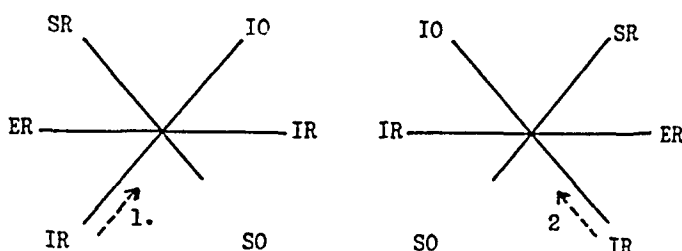


Fig 16—Recession or tenotomy of each inferior rectus for relief of secondary contracture complicating bilateral paralysis of superior oblique muscle

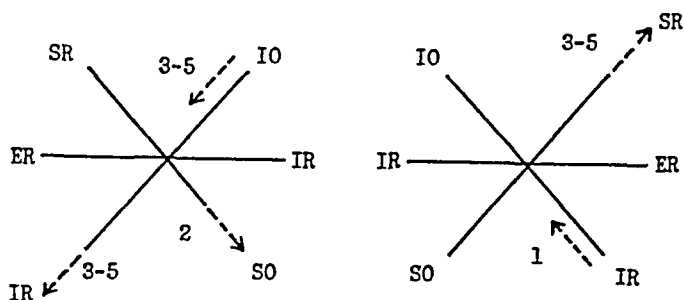


Fig 17—Preferred sequence of combined operations for paralysis of right superior oblique muscle

servative equalization of all depressors, both right and left handed, so as to minimize paralytic cyclophoria and preserve single binocular vision in the lower fields as much as possible

CONCLUSION

It must be realized that no one standard sequence of corrective measures can be advocated for all cases. The plan of attack must be

31 Jaensch cited by Spaeth,²⁴ p 236

based on the measurements in the individual case. It is well to remember that if a choice is permitted weakening of a depressor muscle is undesirable, strengthening of a depressor or weakening of an elevator muscle is preferable, for there is greater need for binocular vision in the lower than in the upper fields. If there is marked overaction of the homolateral, antagonistic inferior oblique muscle, probably tenotomy of this muscle is desirable as the initial operation (fig 8A). In the usual case of paralysis of the superior oblique muscle most surgeons apparently first do a recession of the contralateral inferior rectus and then attempt a shortening of the paralytic superior oblique, especially if the paralysis is of traumatic origin (fig 17). Depending on measurements then obtained, these operations are supplemented by recession of the homolateral, overacting inferior oblique, advancement of the contralateral superior rectus or advancement of the homolateral inferior rectus. In cases of bilateral paralysis of the superior oblique equalization and preservation of the remaining depressors are advisable.

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SURGICAL TREATMENT OF PRIMARY GLAUCOMA

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GLAUCOMA is a pathologic condition of the eye in which an elevation of intraocular pressure results in damage to or even complete loss of vision. It may be stated at this point that treatment should be guided by the damage to function and not, as is often the case, by the state of the intraocular pressure. It is not intended that one should ignore the tension, but it is urged that the greater emphasis be placed on the findings in the visual fields as a criterion for treatment. Every one is familiar with the fact that certain patients maintain a relatively high pressure with little or no loss of visual fields, while others continue to lose field even though the tension is apparently within normal limits.

The treatment of glaucoma is notoriously unsatisfactory. Neither medical nor surgical treatment can be entirely effective until the cause or causes of primary glaucoma are known. Medical treatment should be employed as long as there is no loss of visual fields and the tension can be controlled, but all too frequently one must resort to surgical measures. Surgical treatment should not be delayed too long, since better results follow operation in cases in which the condition is not too far advanced.

What can surgical intervention accomplish? It can increase the outflow of aqueous, and perhaps with diathermy decrease the formation of this fluid. It cannot restore the tension-regulating mechanism to normal, change the vitreous, alter the blood volume in the eye or as yet safely change the rate of aqueous formation.

Three common types of operative procedures are in use.

1 Operation for the relief of acute block of the anterior chamber angle, i e, iridectomy, in cases of acute narrow angle glaucoma.

2 Operation which opens a new intraocular drainage channel, i e, cyclodialysis. This operation is most successful in cases of early chronic wide angle glaucoma, the chronic narrow angle type perhaps and the secondary type which follows cataract extraction.

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Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Dec 17, 1945. The discussion on this paper was published in the May 1946 issue of the ARCHIVES, pages 582-586.

3 Operations which open an extraocular drainage channel, i e, the so-called filtering operations, such as iridencleisis, iridotasis, anterior sclerectomy and corneoscleral trephination. These operations are indicated for all types of primary glaucoma except the early acute narrow angle type, the early chronic wide angle type and, at times, chronic narrow angle glaucoma.

In every case 1 per cent physostigmine salicylate is administered to each eye at least one-half hour before operation. Any operation for glaucoma may be performed with a local anesthetic. Even the iridectomy for acute narrow angle glaucoma may be made with little pain if $\frac{1}{4}$ to $\frac{3}{8}$ grain (16 to 24 mg) of morphine sulfate is given before operation and time is allowed for the retrobulbar injection to act. Cocaine is contraindicated because of its mydriatic action, but 0.5 per cent tetracaine hydrochloride may be substituted for instillation. Then a subconjunctival injection of 2 per cent procaine hydrochloride without epinephrine, followed by a retrobulbar injection of 2 per cent procaine hydrochloride with epinephrine hydrochloride (1:20,000) completes the anesthesia.

IRIDECTOMY

This operation is indicated in cases of early acute narrow angle glaucoma. It is usually successful if the tension can be reduced to normal with miotics or if the acute attack is of not more than three days' duration. If the anterior chamber angle is found to be filled with synechias on visualization with the gonioscope, iridectomy is contraindicated, and one should perform a filtering operation. It is well to reduce the congestion in such an eye before operation if possible.

A keratome incision is contraindicated in iridectomy because the incision is situated too far forward. A shelf of cornea projects in front of the chamber angle and makes it practically impossible to perform a basal iridectomy.

An incision with the Graefe knife is better but is difficult. Fixation must be firm. The puncture begins at 11 o'clock at a point 2 to 3 mm back of the limbus, and, with the blade parallel to and almost against the iris, the knife is carried across the upper portion of the chamber. At 1 o'clock the point of the knife is passed into the chamber angle and the counterpuncture made. This is a stab incision until the knife point emerges from the sclera and conjunctiva on the side of the counterpuncture. Then, with the blade in the same flat position, the knife is swept upward through the sclera and the conjunctiva. The disadvantages of this incision are its technical difficulties, the profuse bleeding, the rapid loss of aqueous and the tendency of the iris to prolapse at once into the incision, thus making it difficult or impossible to perform a peripheral basal iridectomy.

The best operation for acute narrow angle glaucoma is the so-called iridectomy *ab externo*, it is especially good with an extremely shallow anterior chamber. With this technic, the aqueous escapes slowly and the iris does not prolapse into the wound, an iridectomy of the peripheral basal type is easily made, and the operation is not technically difficult. Formerly, some trouble was encountered with fixation, but since scleral fixation sutures have been in use the procedure is simple. After an injection of 2 per cent procaine hydrochloride is made between Tenon's capsule and the sclera, a 5 mm flap of conjunctiva and Tenon's capsule is dissected downward from above the upper portion of the limbus. A fixation suture is then placed by passing a 0000 braided silk suture through the superficial fibers of the sclera 5 mm back of the limbus, cutting the two ends of the suture relatively short and grasping them close to the sclera with a small hemostat. Such an arrangement gives excellent and easily controlled fixation. Remembering that the anterior chamber angle is 1.5 mm back of the limbus, an incision 5 to 6 mm in length is made over this area in a direction parallel to the curvature of the cornea. The incision is made easily and safely with a sclerotome, a Graefe knife or a keratome, with preference for the double-edged sclerotome. An ordinary incision made halfway or more through the sclera is followed by scratching or picking through this coat along the entire length of the incision. One must be careful not to injure the underlying structures. The incision is followed by a peripheral basal iridectomy and replacement of the conjunctival flap. Sutures complete the operation.

CYCLODIALYSIS

This operation has fallen somewhat into disrepute, probably as a result of improper technic followed by a large percentage of failures. It is believed that an insufficient area of the attachment of the ciliary body has been ruptured in many cases and that if almost half the circumference is dialyzed the results are much better.

The operation is indicated in cases of early, and perhaps late, chronic wide angle glaucoma and of the secondary rise of tension following cataract extraction. Furthermore, it is the operation of choice in cases with only a slight elevation of tension, in those with very small visual fields and in many cases in which an external filtering operation has failed to reduce the tension to a normal level.

It is well to make a gonioscopic examination of the chamber angle before operation. This may help one to avoid dense anterior peripheral synechias or large blood vessels in the angle.

Technically the procedure is not difficult, especially if a scleral fixation suture is used. The operation may be done above or below the horizontal meridian, but it is well to avoid the horizontal area in order

to keep away from the long ciliary arteries. If the operation is made below the horizontal meridian, the conjunctiva is incised 5 to 6 mm back of the limbus at a point immediately lateral to the inferior rectus muscle.

A scleral fixation suture of 0000 silk is placed just anterior to the point chosen for the incision. The suture is cut short and grasped near the sclera with a small hemostat. With this suture the globe is well controlled, and if the handle of the hemostat is depressed toward the cornea the anterior lip of the scleral wound is elevated and passage of the spatula is facilitated.

A "scratch and pick" incision, as described for iridectomy ab externo, is made approximately 5 mm behind the limbus and just back of the fixation suture. This incision should be about 5 mm in length in order to allow some play with the spatula.

A blunt spatula is introduced and care exercised to hug the inner part of the sclera as its tip is carried forward into the anterior chamber angle.

The attachment of the ciliary body to the scleral spur is ruptured by pushing in this area, rather than by sweeping. It is well to keep the spatula out of the anterior chamber as much as possible, since the corneal endothelium and Descemet's membrane are easily damaged. Almost one-half the circumference of the attachment of the ciliary body is dialyzed.

Bleeding, if excessive, may be controlled in part by holding a moist absorbent applicator against the scleral wound, even during the dialysis. Also, the spatula and applicator are left in position as long as bleeding continues.

SCLERECTOIRIDECTOMY (LAGRANGE)

Of the external filtering operations, the Lagrange type has been successful most often in this clinic.

The operation is reasonably easy to perform and apparently is followed rarely by cataract. Furthermore, one can combine with it an iris inclusion if a portion of this structure is pulled forward into the scleral opening.

The operation is begun with injection of 2 per cent procaine hydrochloride under Tenon's capsule above the upper portion of the limbus. With dissection thus facilitated, a large, thick flap is made and carried over onto the cornea, as is usually done. Next, a scleral fixation suture, as previously described, is placed in the 11 or 1 o'clock meridian about 5 mm back of the limbus and grasped with a small hemostat. Then a scratch incision approximately 6 mm long is made through the outer coat of the globe 1.5 mm back of the limbus. After completion of the incision, a bite is taken out of the anterior flap of sclera and cornea with

a Holth punch A peripheral basal iridectomy is done, and as a final step the conjunctival flap is sutured

A variation of the operation, i. e., combination with an iris inclusion, is made by grasping the iris midway between the pupillary and the ciliary margin, making an upward snip from a point just below the iris forceps and then laying the flap in the scleral opening

After any filtering operation for glaucoma daily massage helps to establish and maintain filtration This massage is begun on the day following operation and is continued as long as necessary

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RELAPSING AND CHRONIC OCULAR LESIONS

Following Mustard Gas (Dichloroethyl Sulfide) Burns

R O SCHOLZ, M D

AND

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RELAPSING and chronic ocular lesions following mustard gas (dichloroethyl sulfide) burns are reported infrequently in the open literature. There is but 1 such case reported in the American literature¹ and none in the records of the United States Veterans Hospitals². Two hundred and forty-three case reports have been found, 136 give sufficient data for review. Of the cases collected in this paper, 40 are from the open European literature,³ 1 from the American literature,

From the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital and University

1 McKellar, J H. Recurring Kerato-Conjunctivitis Following Exposure to Dichloroethylsulfid, *Am J Ophth* **3** 309-210, 1920

2 Winternitz, M C. Personal communication to the authors

3 (a) Bickerton, R E. New Cases of War Blindness Due to Mustard Gas, *Brit M J* **2** 769-770, 1934. (b) Bonnet, P. Ectasies vasculaires de la conjonctive, reliquat d'une brûlure par ypérite, *Bull Soc d'opht de Paris* **61** 407-409, 1939. (c) Dystrophie de la cornée avec ulcère torpide, manifestation tardive de l'atteinte par ypérite, *ibid* **51** 432-433, 1939. (d) de Courcy, T L. Recurring Keratitis from Mustard Gas Shell, *Tr Ophth Soc U Kingdom* **52** 558-559, 1932. (e) Dor, L, and Fouassier. Suite éloignées des brûlures conjonctivales par l'ypérite, *Clin opht* **26** 183-191, 1932. (f) Fairclough, W A. Gas Keratitis, *Australian & New Zealand J Surg* **7** 163-166, 1937. (g) Genet, L. Ypérite, ischémie conjonctivale, ulcère cornéen tradif, *Bull Soc d'opht de Paris* **49** 409-412, 1937. (h) Heckford, F. Delayed Corneal Ulceration Following Mustard Gas Burns, *Proc Roy Soc Med* **30** 949, 1937. (i) Jacqueau, A, and Bujadoux, A. Infection aiguë et spontanée des deux globes oculaires, à deux ans d'intervalle, chez un ancien ypérite, *Bull Soc franç d'opht* **38** 370-380, 1925. (j) Pesme, P. Fistula de la cornée consecutive à brûlure par l'ypérite, *Arch d'opht* **41** 278-283, 1924. (k) Moore, R F, and Heckford, F. Delayed Corneal Ulceration from Mustard Gas, *Brit M J* **1** 497-498, 1929. (l) Neame, H. Late Result After Mustard-Gas Burn of the Eye, *Proc Roy Soc Med* **22** 25-26, 1928. (m) Parlange, J A. Les sequelles oculaires des gaz de combat, *Arch d'opht* **46** 87-119, 1929. (n) Ridley, H. Mustard Gas Keratitis, *Proc Roy Soc Med* **29** 962-963, 1936. (o) Rohrschneider, W. Spatschädigung der Augen nach Gelbkreuzgas-

(Footnote continued on next page)

9 from the duplicate records of the Evergreen School for the Blind in Maryland (1918 to 1924), an institution to which all of the United States Army blind of World War I were sent after the close of hostilities, and 2 were submitted from private practice ⁴ Recently Mann ⁵ analyzed 84 cases from one London hospital

The 107 cases not included in this review are mentioned only briefly in the literature,⁶ and the data are insufficient for analysis

ANALYSIS OF CASE REPORTS

The original records of the patients are usually not accessible, the few which are available are incomplete because of combat conditions. The available data for the cases reviewed are summarized in table 1

The cases may be roughly divided into three groups. The first group consists of the 24 cases, 16 summarized in table 1 and 8 mentioned by Mann, in which the course was a chronic one, with exacerbations and remissions. The second group consists of 96 cases, 20 summarized in table 1 and 76 studied by Mann, in which there were recurrences from five months to twenty-six years after the original lesion had apparently healed. The third group comprises 16 cases (table 1) in which the available data do not permit classification.

Mann ⁵ saw no case of delayed keratitis in which the initial ocular symptoms lasted less than six weeks. In the literature reviewed here, the exact nature and extent of the original burn could not be determined, but from the reports in which sufficient detail was given it was noted that the initial lesions were severe and hospitalization was prolonged.

From the available clinical data, no essential difference could be found between the ocular lesions in the cases of chronic and those of the recurring type, so they will be described together.

The usual presenting symptoms were severe photophobia and lacrimation with frequent diminished visual acuity. On examination the conjunctiva was found to be congested except in the intrapalpebral fissure, where, adjacent to the limbus, there were porcelain white

Vergiftung, *Klin Monatsbl f Augenh* **99** 447-455, 1937 (*p*) Šrytr, F. Varätzung mit Yperite, *Oftal sborn* **5** 215-222, 1930, (*q*) *Zentralbl f d ges Ophth* **24** 334-335, 1931 (*r*) Sourdille, G. P. Troubles corneens et lesions vasculaires du limbe chez un yperite, *Bull Soc d'opht de Paris* **48** 799-801, 1936 (*s*) Weill, G. Ulceres tradifs de la cornee chez un ancien yperite, *ibid* **51** 281-282, 1939 (*t*) Zettl, W. Zur Symptomatologie und Therapie der Spätschädigungen des Auges durch Gelbkreuzgas, *Klin Monatsbl f Augenh* **104** 217-222, 1940

4 (*a*) Burke, J. W. Personal communication to the authors. (*b*) Friedenwald, J. S. Personal communication to the authors.

5 Mann, I. Report on a Follow-up Investigation of Eighty-Four Cases of Delayed Mustard Gas Keratitis, personal communication to the authors.

6 Ratnaker, R. P. A Case of Nystagmus Caused by Mustard Gas, *Lancet* **1** 423-424, 1919. Parlange sm

ischemic areas surrounded by dilated irregular veins. In 6 of the reported cases only the conjunctiva was involved ^{3m}

In the majority of cases, 74 in Mann's series and 44 of the 52 cases summarized in table 1, the corneal lesions ranged from mild superficial keratitis to a corneal fistula ^{3j} and perforated corneal ulcers ⁷

The ulcers were described as being of various depths, sizes and locations but usually occurred in the palpebral fissure at the limbus. The margins of the ulcers were raised and irregular. The tissue immediately surrounding the ulcer was necrotic. In some cases calcification took place. The clinical course of these ulcers was one of frequent remissions and exacerbations. Secondary iritis occurred in 5 cases and glaucoma in 2 cases. The distribution of the complicating lesions in the various groups is shown in table 2.

Some of the patients had fair visual acuity following the healing of the initial burn and lost vision completely only as the result of subsequent attacks.

Excluding the cases of mild conjunctival involvement reported by Parlange,^{3m} in which there was practically no loss of visual acuity, average loss of vision in the remaining cases in table 1 was approximately 88 per cent. This visual disability presents a medicolegal problem. Unless the recurrent nature of mustard gas burns is understood, the examining physician may ascribe the ulcers to another cause, and the patient may be thus deprived of his disability compensation.

Until the recent successful use of contact lenses to treat patients with such lesions ⁸ therapy on the whole has been unsatisfactory. Local treatment with diathermy, antiseptic and anesthetic ointments and atropine has been most frequently given. Nonspecific protein therapy has been tried, without success.

Enucleation was necessary in 4 cases. A Saemisch section was tried in 1 case, without success ³ⁱ. Closure of the corneal fistula in Pesme's case was accomplished by electrolysis. Curettage of the corneal ulcer was successfully performed in some of the cases reported in table 1 ⁹ and in some of Mann's cases.

Tarsorrhaphy was tried in 4 of the cases tabulated here but was successful in only 1. This treatment was also successful in Duke-Elder's cases, which are not reviewed here, and was advised by Phillips ^{8a} and Mann ⁵ in their reviews. Bickerton,^{3a} on the other hand, advised against this treatment.

7 Bickerton ^{3a} Jacqueau and Bujadoux ³ⁱ

8 (a) Phillips, T. J., in Discussion on Gas Injuries to the Eye, Proc. Roy. Soc. Med. **33** 229-232, 1940, (b) personal communication to the authors. (c) Duke-Elder, W. S. Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2.

9 Friedenwald ^{4b} Moore and Heckford ^{3h}

TABLE 1—Summary of Case Histories in Present Series

Author	Case Number	Source of Material	Salient Clinical Information	Final Visual Acuity
Bickerton ^{2a}	1	Literature	A Chronic Lesions Gassed in 1918, 9 mo in hospital thereafter, steady visual loss. Marked retinal degeneration and pigmentation noted in 1935	R E 1/200 L E 1/2/200
	2	Literature	Gassed in 1918, 4 mo in hospital, eyes have 'troubled' since L E broke down in 1929 and again in 1933, R E ulcerated in 1933, both eyes treated with tarsorrhaphy, ulcerations continued	R E 1/60 L E Loss
	3	Literature	Patient gassed in 1917, 7 mo in hospital, under treatment since 1934. R E corneal nebula iritis, L E intense photophobia, corneal nebula	R E 3/60 L E 1/200
	4	Literature	Gassed in 1918, eyes never recovered 1934 bilateral corneal ulceration, tarsorrhaphy in left eye. Recurrences of ulceration every six weeks	R E 2/60 L E Loss
	5	Literature	Gassed in 1915, 6 mo in hospital. Both corneas badly burned, patient under treatment since, vision still deteriorating	R E ? Light perception L E 1/60
Parlange ^{3m}	1	Literature	Gassed in 1918, continuous conjunctival irritation to 1925, no corneal involvement	R E 20/20 L E 20/20
	2	Literature	Gassed in 1918, chronic conjunctival infection with exacerbations, small corneal pannus	R E 20/30 L E 20/30
	3	Literature	Gassed in 1918, chronic conjunctival irritation until 1926, no corneal involvement	R F 20/30 L E 20/70
	4	Literature	Gassed in 1918, chronic conjunctival infection with signs of irritation at times	R E 20/30 L E 20/30
	5	Literature	Gassed twice in 1918, chronic conjunctivitis, particularly when fatigued, no corneal involvement	R E 20/20 L F 20/20
Woods	1	Evergreen School for the Blind	Gassed in 1918 slight impairment of vision with subsequent chronic inflammation 1920 R F follicular conjunctivitis and corneal nebula L E violent deep purple connection of conjunctiva, thickening of lids, corneal nebula	R E 1/60 L E Hand movements
	2	Evergreen School for the Blind	Gassed in 1918 sight failed steadily thereafter 1920 R F anophthalmos, L F keratoconjunctivitis with secondary glaucoma	R F 0 L E 0
	3	Evergreen School for the Blind	Gassed in 1918, L 1 weak thereafter and lacrimating, with subsequent complete blindness, enucleated	R E 20/70 L F 0

	4	Evergreen School for the Blind	Gassed in 1918, continued failure of vision R E chronic congestive glaucoma with acute exacerbation, enucleation L E old amblyopia ex anopsia	R E 0 L E 2/30
	5	Evergreen School for the Blind	Gassed in 1918, continual symptoms in warm weather, bilateral corneal ulceration in 1919 1920 R E deep conjunctival congestion with follicles, corneal nebulas, L E opaque cornea, superficial clouding, vascularization	R E Hand movements L E 2/60
	6	Evergreen School for the Blind	Gassed in 1915, recurrent conjunctivitis thereafter 1920 R E conjunctival congestion with tendency to dry folliculosis, cornea practically clear, organized exudate on anterior capsule of lens, L E fibrous tag across pupil, exudate over anterior capsule Other evidence of old iritis	R E 2/60 L E 2/30
	B Recurrent Lesions			
Bonnet ^{3b c}	1	Literature	Gassed in 1918, severe conjunctival burns, vision lowered 2 yr 1937, R E bulbous keratitis, L E serpyiginous ulcer of cornea and hypopyon	R E 0 L E 0
Burke ^{4a}	1	Private practice	Gassed in 1917, invalidated for 6 mo 1937 corneal ulcer in L E 1940 corneal ulcer in R E	R E 18/20 L E 20/50
Fairclough ^{3f}	1	Literature	Gassed in 1917, corneal nebulas present 1 mo after burn, patient returned to service 1930 shallow ulcer of cornea with photophobia and lacrimation 1936 R E irritated, corneal sensitivity diminished, L E chronically congested conjunctival vessels	R E Not given L E Not given
	2	Literature	Patient gassed in 1918, hospitalized 63 days with keratoconjunctivitis, condition quiet until 1924, vision then 6/36 (O U) 1924 bilateral conjunctivitis, nebulous corneas with calcareous deposits Evidence of old iritis	R E 6/60 L E 6/60
	3	Literature	Gassed in 1917, severe conjunctivitis, lacrimation and photophobia 1920 patient well, with 6/5 vision (O U) 1933 recurrence in R E 1936 L E blind, painful, enucleated	R E Not given L E 0
Genet ^{3g}	1	Literature	Patient gassed in 1916, well until 1931, when corneal ulcers appeared; several remissions and exacerbations 1936 R E injected vessels and corneal leukoma, L E intense congestion except for ischemic area and small epithelial corneal ulcer, which did not heal within 1 yr	R E Not given L E Not given
Hockford ^{3h}	1	Literature	Apparent early recovery from first burn 1932, recurrence with porcelain white appearance of conjunctiva, injected vessels, loss of corneal substance Diminished corneal sensation over scarred areas	R E 6/18 L E 6/24
Jacquau and Bujadoux ³ⁱ	1	Literature	Gassed in 1918, vision decreased for 6 mo, then slowly improved 1922 R E sudden development of corneal ulcer with subsequent panophthalmitis and enucleation, L E corneal ulcer 1 mo later with enophthalmos	R E 1/10 L E 1/13

TABLE 1—Summary of Case Histories in Present Series—Continued

Author	Case Number	Source of Material	Salient Clinical Information	Final Visual Acuity
McKellar ¹	1	Literature	Gassed in 1918, inflammation lasted 6 wk. 1919 fourth recurrent attack of corneal ulceration, R E conjunctivitis, L E normal in 1 mo	R E Not given L E Not given
Parlange ^{3m}	1	Literature	Patient gassed in 1918, well to 1921, then recurrent conjunctivitis, old corneal scars	L E 20/30 R E 20/30
	2	Literature	Gassed in 1918 (probably by mustard gas), recurrent conjunctivitis, in 1928 cicatricial keratitis	R E 20/100 L E Not given
	3	Literature	Gassed in 1917, conjunctiva infected at various times 1928, infected conjunctiva and small corneal opacity	R E 20/20 L E 20/20
	4	Literature	Gassed in 1918 1928 conjunctivitis, small pannus	R E 20/15 L E 20/15
	5	Literature	Gassed in 1918 (probably lacrimal and mustard gas), repeated attacks of conjunctivitis	R E 20/30 L E 20/30
Ridley ³ⁿ	1	Literature	Patient gassed in 1918, blind for 10 days, vision normal in 1919 and 1921 1936 recent diminution of vision, bilateral corneal opacities in palpebral fissures corneal fissures reduced	R E 6/60 L E 6/60 L E 6/60
Rohrschneider ^{3o}	1	Literature	Gassed in 1918, no definite evidence of corneal damage, complete recovery 1933 bilateral degenerative keratitis	R E 10/200 L E 30/200
Sourdille ^{2r}	1	Literature	Gassed in 1918 1933 severe conjunctival lesions 1936 R E keratitis L E superficial keratitis	R E 20/200 L E Not given
Well ^{3a}	1	Literature	Gassed in 1918, no trouble until 1937, then marginal corneal ulcers without pain or injection	R E Not given L F Not given
Woods	1	Evergreen School for the Blind	Gassed at drill in 1919 (kind of gas?) vision improving since 1921 R E chronic conjunctivitis L E old iritis and immature cataract	R F 2/60 L E 2/30
Zettl ^{3t}	1	Literature	Gassed in 1918 corneal burn, decreased visual acuity No complaints to 1924, then recurrence of irritation 1935 corneal ulcer 1939 corneal ulcer in R F with Denigk transplant vision improved from counting fingers at 1 ft to 6/200	R E 6/200 L F 20/20
	C Cases Not Classified			
Blockerton ^{3a}	1	Literature	Gassed in 1918 corneal ulcers and nebulas in both eyes 1931 recurrence of inflammation and ulceration	R E 1/60 L E 1/60
	2	Literature	Gassed in 1918 1934 R F perforated corneal ulcer L E lower half of cornea opaque Evidence of old iritis	R E 0 L E Light perception

Bonnet 3 ^b c	1	Literature	Gassed in 1917, no symptoms, even in 1937, vascular ectasis of conjunctiva. Biopsy of conjunctiva revealed dilated vessels and fibrous tissue	R E L E	Not given Not given
Dor and Fouassier 3 ^e	1	Literature	Gassed in 1918, treatment for leukoma of both corneas with ulcers for 14 mo	R E L E	Not given Not given
	2	Literature	Gassed in 1918, 3 mo rest required, much photophobia and lacrimation	R E L E	Not given Not given
de Courey 3 ^d	1	Literature	Liquid splash burn in 1917, keratitis 6 mo, diminished vision in R E 1925 R E keratitis "flared up" for over a year, partial tarsorrhaphy, L E keratitis flared up, both corneas hyposensitive 1932 condition in R E again flared up, crystals in both corneas	R E L E	6/60 6/9
Fisher	1	Literature	Patient seen in 1928, with bilateral hypopyon ulcers, condition helped by tarsorrhaphy	R E L E	Not given Not given
Friedenwald 4 ^b	1	Private practice	Gassed in 1918, right eye severely burned 1929 recurrent ulcers, R E helped by curettage, L E irritated but not ulcerated	R E	Not given
Moore and Heckford 3 ^k	1	Literature	Gassed in 1917 1928 deep, gutter like excoriation of cornea, small ulcers at limbus	R E L E	Not given Not given
	2	Literature	Gassed in 1917, 1922 ulceration of L E, with formation of nebulas, recurrence 1928 corneal ulcer curetted, slowly healed over in 7 mo	R E L E	Not given Not given
Neume 3 ^l	1	Literature	Gassed in 1918, 3 mo in hospital 1928 R E pallor around cornea, engorgement of vessels peripheral to this, L E hypopyon ulcer, Saemisch section, eye blind	R E L E	Not given 0
Parlange 3 ^m	1	Literature	Gassed in 1918 1928 dilated vessels and corneal anesthesia	R E L E	20/20 20/20
Pesme 3 ^j	1	Literature	Gassed in 1918 1924 L E vision decreased, owing to keratitis, subsequent development of fistula, which was closed with electrolysis needle, R E healed keratitis	R E L E	4/10 Not given
Srytr 3 ^p	1	Literature	Splash burn on cheek in 1918, immediate neutralization 5 mo later R E showed irritation of lower cornea with deep vascularization and hemorrhage	R E L E	Not given Not given
Woods	1	Evergreen School for the Blind	Gassed twice in 1918, blind 2 yr after, 1921 recurrence of great conjunctival congestion, lacrimation and photophobia	R E L E	Counting fingers Counting fingers
	2	Evergreen School for the Blind	Gassed in 1918, poor vision since 1921, conjunctival congestion with tendency to dry folliculosis, organized exudate on anterior capsule of both lenses Corneas practically clear	R E L E	2/60 2/30

Ida Mann, in her excellent review in 1944,⁵ reported the most beneficial results to date from the use of contact glasses. She stated that "the history of a long interval, followed by repeated ulcers and fluctuating but slowly deteriorating visual acuity, which is relieved by wearing contact glasses, is typical of roughly 46 per cent of the cases." In all but 2 of her cases conspicuous improvement in visual acuity followed the use of contact lenses. Because of this notable increase in visual acuity, together with the relative insensitivity of their corneas, the patients had good tolerance for the contact glasses, almost half wearing the lenses throughout the working day.

Phillips, likewise, had remarkable results not only in healing recurrent ulcers but also in improving vision with the use of contact glasses.

TABLE 2—*Summary of Late Complications Found in Cases of Relapsing Mustard Gas Lesions of the Eyes*

Complications	Chronic Lesions (24)	Recurrent Lesions (96)	Cases Not Classified (16)
Corneal ulcers	5	14 74 (Mann)	10
Conjunctivitis			
Chronic	5	6	2
Follicular	2		1
Iritis	3		2
Cataract		1	
Glaucoma			
Acute	1		
Chronic	1		
Retinitis	1		
Choroiditis			
Insufficient data	9		

The use of corneal transplants in treatment of these lesions has not been reported but may be of value. It is also suggested that the scars may be cleared by the injection of an enzyme preparation which will strongly hydrolyze hyaluronate and chondroitin sulfate.¹⁰

ETIOLOGIC FACTORS

The etiologic factors most applicable to the production of relapsing mustard gas injuries, as taken from the review of Hughes¹¹ and from the more recent literature, are (1) tissue sensitivity, (2) destruction of the mucous glands, (3) corneal anesthesia, (4) vascular abnormalities, (5) cholesterol crystals and (6) loosening of the corneal epithelium.

10 Meyer, K, and others. The Effects of Intracorneal Injection of Hyaluronic Acid and Its Monosulfuric Acid Ester, The Action of Testicular Enzyme Preparations on Corneal Opacities, personal communications to the authors.

11 Hughes, W F, Jr. Mustard Gas Injuries to the Eyes, Arch Ophth 27:582-601 (March) 1942.

Tissue Sensitivity—Sollmann,¹² after experiments on human beings, concluded that "healed mustard burns are over-susceptible to injury, mechanical or chemical, and therefore incidentally to mustard" He expressed the belief that uninjured skin does not become sensitive to mustard gas As the patients in the present series were not again exposed to this gas, the recurrences might conceivably have been due to auto-sensitivity to altered corneal proteins That specific antigens may be obtained from serum treated with mustard gas was shown by Berenblum and Wormall¹³

Destruction of Mucous Glands—Bickerton^{3a} suggested that the changes in the tissue resulted from lack of a lubricating substance after destruction of the mucus-secreting glands of the conjunctiva Warthin and Weller,¹⁴ in their studies on the pathologic changes in rabbit eyes burned with mustard gas, showed that there is involvement of the conjunctival epithelium in which the mucous glands are located but that the epithelium is rapidly regenerated From the clinical data no evidence of lack of lubricating secretions is found, and the unexposed portions of the conjunctiva could be expected to furnish their normal contribution of mucus

Corneal Anesthesia—The cornea was reported to be anesthetic in many of the cases, and Fairclough^{3f} mentioned this as characteristic of recurrent mustard gas lesions If the recurrent or relapsing lesion is caused by a mechanism similar to that of neuromyolytic keratitis, it is remarkable that it does not occur more frequently in conditions in which hypesthesia of the cornea is also present

Vascular Abnormalities—The ischemic areas in the conjunctiva, the "marbled veins" and the necrotic chronic ulcers suggest absence of adequate blood supply as a cause While the conjunctival vessels normally may be responsible for some part of the nutritive supply of the cornea, the major supply of metabolites normally comes from the aqueous and from oxygen of the outside air

Cholesterol Crystals—Mann and Pullinger¹⁵ suggested that the recurrent lesions may be caused by cholesterol crystals working their way to the surface and causing ulceration of the epithelium They

12 Sollmann, T Dichlorethyl Sulphid ("Mustard Gas"), J Pharmacol & Exper Therap **12** 303-321, 1919

13 Berenblum, I, and Wormall, A The Immunological Properties of Proteins Treated with β β^1 -Dichlorodiethylsulphide (Mustard Gas) and β β^1 -Dichlorodiethylsulphone, Biochem J **33** 75-80, 1939

14 Warthin, A S, and others The Ocular Lesions Produced by Dichloroethylsulphide, J Lab & Clin Med **4** 785-832, 1918

15 Mann, I, and Pullinger, B D The Pathological Effects of Mustard Gas on the Eye of the Rabbit, personal communication to the authors

observed these crystals being deposited along the vessels which invade the cornea contaminated with mustard gas in experimental animals

Loosening of the Epithelium—It has been observed in experimental mustard gas lesions of the eye that the epithelium which grows over the damaged stroma is loosely attached and remains so until the stroma returns to normal¹⁶ This loosely attached epithelium is easily rubbed off, exposing the underlying abnormal stroma to infective agents This sequence, which we have frequently observed in experimental animals, may well be the mechanism by which relapsing keratitis is caused in man

SUMMARY AND CONCLUSION

One hundred and thirty-six cases (including 84 reported by Mann) of chronic and recurring mustard gas burns of the eye have been collected and analyzed No essential difference is found between cases of the chronic and cases of the recurrent type In the average case there were few, if any, complete remissions, and the condition progressed steadily over one or more decades to serious visual loss The lesions had a characteristic clinical appearance They were usually bilateral and involved chiefly the exposed palpebral aperture The conjunctiva generally showed a marbled appearance, with ischemic areas surrounded by dilated, tortuous veins of irregular caliber The corneal ulcers, when they occurred, might be shallow or deep and might occur at any location on the cornea, frequently at the limbus The edges of the ulcers were raised and irregular In some cases the scars became partially calcified

No universally beneficial treatment has been reported Curettage of the diseased corneal tissue and tarsorrhaphy seem to have been somewhat efficacious in shortening the duration of the relapse Corneal transplants have not been tried and may be of benefit The use of contact glasses to promote healing of the recurrent ulcers and to improve the patient's vision has been the most successful treatment reported

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16 Scholz, R O Clinical and Pathological Studies of Ocular Mustard Gas Burns, unpublished data

A SQUINT SYNDROME

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IN 1934 Braun ¹ called attention to the fact that the normal "blindspot," resulting from the absence of perceptive elements in the optic papilla, may form the nucleus of a suppression scotoma in the squinting eye. Seven cases of esotropia are now reported as representative of a clinical entity in which the physiologic blindspot seems to play an exceptional role as a central scotoma in the squinting eye. Recognition of the "blindspot" syndrome is important because it seems common and remediable. Restoration of comfortable single binocular vision results if treatment is properly directed, whereas partial or improper measures are of little benefit and may add to the patient's distress.

Recognition of this syndrome resulted from determination of the field of binocular vision in 296 cases of concomitant esotropia in older children and adults. The field of binocular vision was plotted by the use of colored filters and twin projection systems of the type described by Lancaster ². For example, a red filter was placed before the fixating eye, and for a fixation point a small red disk of light was projected onto an unmarked white screen. A green filter was placed before the squinting eye and a green disk of light projected on the screen at various positions to plot the field of vision of this eye. The fixating eye viewed only the red light and the squinting eye only the green light. The patient was not required to distinguish the color of the peripheral green image, but was asked only to perceive a second light. This method permitted plotting of the fields of vision at fixation distances of 0.5 to 6 meters. The test was performed in an illuminated room to simulate as nearly as possible the conditions under which the eyes are used normally. For the proper interpretation of such a test, the deviation of the eyes and the state of retinal correspondence had to be known. The deviation of the eyes during the test was measured by corneal reflex (Priestley Smith tape and perimeter) and prism cover test methods.

From the Departments of Ophthalmology, the University of Oregon Medical School and the State University of Iowa College of Medicine.

1 Braun, G. Gesichtsfelduntersuchungen bei Schielenden, *Klin Monatsbl f Augenh* **92** 600-613 (May) 1934.

2 Lancaster, W. B. Detecting, Measuring, Plotting and Interpreting Ocular Deviation, *Arch Ophth* **22** 867-880 (Nov) 1939.

The state of the retinal correspondence was determined by the major amblyoscope and after-image tests, as well as by the red-green method³

In accordance with the finding of Travers,⁴ the "object of regard," that is, the point of fixation and the immediately surrounding area, seemed to be perceived monocularly in most cases of long-standing untreated concomitant esotropia. Travers expressed the belief that this monocular perception of the "object of regard" was due to suppression of the image in the peripheral retina of the squinting eye, however, in many of my cases it was demonstrated that rays of light from the objects fixated by the fovea of the fixating eye fell on the optic papilla of the squinting eye. In such instances, an absolute scotoma, the physiologic blindspot, was provided by nature. Esotropia of 12 to 17 degrees for distance fixation results in the areas in the field of binocular vision corresponding to the fovea of each eye being overlapped by the physiologic blindspot of the opposite eye.

In 80 of my 296 cases of concomitant esotropia, the physiologic blindspot of the squinting eye was found to overlie the point of fixation when measured at distances of 0.5 to 6 meters with the color filter projection method previously described. It was impossible in most of these cases to do more than theorize as to the possible role played by the physiologic blindspot because it was only part of a large scotoma in the squinting eye. There were, however, 7 cases in which it seemed probable that the physiologic scotoma alone provided a mechanism for partial alleviation of diplopia. In these 7 cases the blindspot of each eye consistently overlapped the central area of the opposite eye at all distances of fixation, and no other scotoma could be plotted in the field of binocular vision. The pertinent features, treatment and course in each of the 7 cases are presented.

CASE 1—A 15 year old white girl had acquired convergent strabismus associated with diplopia at the age of 7 years. When she was 10, glasses were prescribed, and a recession of the medial rectus muscle of the right eye was performed by an ophthalmologist. The deviation appeared to be corrected, but postoperative diplopia was so annoying that it was necessary for the child to withdraw from school. Disappearance of constant diplopia six months later was associated with return of the strabismus. At the time of my examination the patient still had periodic diplopia and a concomitant esotropia of 14 to 16 degrees for distance fixation. Cycloplegic refraction revealed 3 D of hyperopia and 1 D of astigmatism in each eye. Visual acuity was 20/20 in each eye with correcting lenses. The only scotomas which could be plotted in her fields of binocular vision with the color filter projection method were the normal physiologic blindspots. The blindspot of the squinting eye was found to overlie the point of fixation at all fixation distances from 0.5 to 6

3 Swan, K. C. Definition of Anomalous Retinal Correspondence, *Am J Ophth* **28**: 58-61 (Jan) 1945

4 Travers, T. a'B. The Origin of Abnormal Retinal Correspondence, *Brit J Ophth* **24**: 58-64 (Feb) 1940

meters Retinal correspondence was normal with the after-image test Diplopia was constant with prisms partially correcting the deviation, however, with the major amblyoscope adjusted to correspond to the deviation, the patient was able to fuse even the most complex picture targets with a convergence-divergence amplitude of 5 to 7 D and described stereopsis Corrective lenses were prescribed and daily orthoptic exercises initiated with the major amblyoscope A convergence-divergence amplitude of 25 D developed after several weeks of training, but the deviation remained unchanged A 5 mm recession of the medial rectus muscle of the left eye was then made Postoperatively, the patient was able to maintain single binocular vision for fixation beyond 0.5 meter, but several months of daily home training with the Brewster-Holmes stereoscope was required to establish comfortable single binocular vision for reading At the completion of this period, with the Maddox rod the patient had 2 D of esophoria for distance and 1 D of esophoria for near fixation There was no hyperphoria Prism convergence was 25 D and divergence 5 D The vertical vergences were 3 D The patient was able to bar read She did her school work comfortably and had no change in status during the three years that she was observed after operation

CASE 2—A 9 year old boy had had convergent strabismus since infancy When the boy entered school, at the age of 7, he had difficulty in learning to read and described double vision An optometrist prescribed glasses and "exercises," but the eyes remained crossed and periodic diplopia persisted Examination on his admission revealed uncorrected visual acuity of 20/20 in each eye, but with cycloplegia he had 2 D of hyperopia There was an alternating concomitant esotropia of 12 to 17 degrees for distance fixation In the field of binocular vision the point of fixation was overlapped by the blindspot of the squinting eye at all distances Retinal correspondence was normal with the after-image test With the major amblyoscope, the patient was able to fuse various standard slides after the targets were adjusted in the instrument to correspond to the deviation of the eyes, but his amplitude of fusional movements was limited to a few diopters Lenses and orthoptic exercises were prescribed Six weeks later, when he had acquired an amplitude of fusional movements of 15 D on the major amblyoscope, a recession of 5 mm was done on the medial rectus muscle of the left eye This procedure effected only a partial correction of the deviation, and as a result diplopia was constant postoperatively An occluder was prescribed for one eye, which was worn except when he was taking orthoptic exercises with a prism stereoscope Two months after the first operation a recession was performed on the medial rectus muscle of the right eye The patient had single binocular vision under room conditions on the first postoperative day No deviation was perceptible with the cover test, and with the Maddox rod he had only 1 D of esophoria for distance and 2 D of exophoria for near fixation Prism convergence was only 7 D and prism divergence 2 D, therefore, orthoptic exercises were continued at home for a month after operation At the end of that period prism convergence had increased to 12 D, and the patient was able to bar read He was able to read with comfort and progressed rapidly in school during the following two years of observation

CASE 3—A boy aged 11 was referred to me with a diagnosis of "horror fusionis" Convergent strabismus had been present since infancy When the boy started school, he had difficulty in learning to read because of periodic double vision Glasses correcting his 3 D of hyperopia did not seem beneficial, therefore, the attending ophthalmologist did a recession on the medial rectus muscle of the right eye Postoperative diplopia was constant and necessitated the boy's with-

drawal from school for a year. At the end of this period the eyes had returned to the squinting position and the diplopia had become periodic. My examination, two years later, revealed concomitant esotropia of 14 to 16 degrees for distance fixation, with overlapping of the point of fixation by the physiologic blindspot of the squinting eye. Diplopia could be created under room conditions by partially correcting the deviation with prisms. Retinal correspondence was normal in the after-image test. With the major amblyoscope adjusted to the deviation of his eyes, the patient was able to fuse even the most complex stereoscopic targets, but his amplitude of divergence and convergence was limited to several diopters. Monocular occlusion was prescribed, and orthoptic exercises were initiated to develop a large amplitude of fusional movements before operation. After fourteen orthoptic sessions of thirty minutes each with the major amblyoscope he was able to fuse the standard stereoscopic targets over a range from 16 to 27 degrees of convergence. A recession of the medial rectus muscles was then performed, which reduced the deviation to 2 degrees of esophoria. On the first postoperative day the boy had single binocular vision for all objects beyond 1 meter. After one week of orthoptic training he was able to fuse larger objects at 30 cm but was unable to read fine print with both eyes without a spasm of accommodation. At the end of two weeks of orthoptic training he was able to read the finest newspaper print through a bar reader. When last seen, one year after operation, the boy had comfortable single binocular vision. With the Maddox rod, he had 2 D of esophoria for distance and 1 D of exophoria for near fixation. Prism divergence was 4 D and prism convergence 14 D. One diopter of left hyperphoria was corrected by incorporating a prism in his glasses. Stereopsis was present.

CASE 4—An 8 year old boy had had crossed eyes since infancy. Glasses had been prescribed when he was $2\frac{1}{2}$ years old, and an operation had been performed on the right lateral rectus muscle at the age of 5 years, but no improvement was noted. When the boy started school, at the age of 7, he complained periodically of diplopia. Exercises with a prism stereoscope were begun under the supervision of an ophthalmologist but were discontinued when no benefit was evident. One year later the patient was admitted to my service with the complaint of double vision and inability to read comfortably without closing one eye. The pertinent findings were a refractive error in each eye of 1 D of hyperopia associated with 1 D of astigmatism and right concomitant esotropia of 13 to 15 degrees for distance fixation, and overlapping of the fixation point by the blindspot of the right eye. Under room conditions, diplopia resulted with 30 D of prism base out, but with the major amblyoscope adjusted to from 11 to 16 degrees of convergence the boy was able to fuse even the most complex stereoscopic targets. Retinal correspondence was normal in the after-image test. Correcting lenses were prescribed, and a recession of the medial rectus muscle of the right eye was made after two weeks of orthoptic exercises. When the bandages were removed, on the second postoperative day, the patient had single binocular vision. With the Maddox rod he had 1 D of esophoria for distance and 3 D for near fixation. There was no vertical deviation. Prism convergence was 16 D, and prism divergence was 4 D. He was able to read after several days of intensive orthoptic training. Further orthoptic exercises were considered unnecessary, for the boy had comfortable single binocular vision and a large reserve of fusional movements. Reexamination a year later revealed no change in his status.

In the successful treatment of the preceding 4 patients, corrective lenses, orthoptic measures and surgical procedures were utilized fully. In the following 2 cases partial measures were attempted.

CASE 5—A girl aged 14 had had convergent esotropia and periodic diplopia since the age of 4 years. Repeated changes of glasses did not seem to affect the deviation or diplopia, an operation was therefore performed by an ophthalmologist when the child was 8 years of age. After operation, the patient had constant diplopia until the squint returned to its former deviation, three months later. The parents were so discouraged that no further care was given the patient's eyes until my examination, six years later. With cycloplegia, the right eye was found to have 2 D of hyperopia and the left eye 4 D of hyperopia with 2 D of astigmatism. Maximal visual acuity was 20/20 in the right eye and 20/20—5 in the left eye. The deviation and other measurements were otherwise similar to those in the preceding cases. Orthoptic treatments were not possible, for social and economic reasons, therefore, after correcting lenses had been worn for three months, operation was performed, at the family's insistence for purely cosmetic reasons. Recession of the medial rectus muscle of one eye resulted in reduction of the deviation to 3 degrees of esotropia. Constant diplopia was evident on the first postoperative day and persisted for about six weeks. Reexamination two months after operation revealed that the deviation was only 2 degrees less than that measured preoperatively. The parents were dissatisfied and refused further treatment.

CASE 6—A girl aged 19 had a history similar to that in the preceding cases, that is, one of convergent strabismus and periodic diplopia, not benefited by the usual procedures. At the age of 8 and again at the age of 13 she had undergone operation for esotropia. Each operation had been followed by a period of partial correction of the deviation associated with constant diplopia. The clinical findings were similar to those in the preceding cases except for a larger degree of anisometropia. Her refractive error was less than 1 D of simple hyperopia in the left eye and 3 D of hyperopic astigmatism at an oblique axis in the right eye. I advised the patient that another operation, as well as orthoptic measures and lenses, would be required before her eyes could be corrected. She refused treatment because of her previous unfortunate experience with operations.

CASE 7—A medical student aged 24 stated that his eyes had been crossed in childhood but had been corrected with glasses. He stated that he had had diplopia for years but it bothered him only when he "thought about it." Examination revealed concomitant esotropia of 12 to 14 degrees for distant fixation, associated with $4\frac{1}{2}$ D of hyperopia and $1\frac{1}{2}$ D of astigmatism in each eye. Visual acuity was 20/20 with correction. Retinal correspondence was normal. Overlapping of the fixation point by the normal blindspot of the squinting eye could be plotted accurately with the red-green projector system. No treatment other than the prescription of glasses was undertaken in this case because the patient had learned to compensate for his diplopia and the cosmetic defect was not conspicuous. The deviation was less apparent because the patient had a positive angle gamma of 2 degrees in each eye, a wide interpupillary distance and prominent eyes.

COMMENT

The similarity in histories and clinical findings in the afore-described cases is striking, however, other features may be evident when additional cases are studied by methods other than those which I used. Certainly, 7 cases do not constitute an adequate series from which to draw conclusions concerning therapeutic measures, but it is noteworthy that in 4 of the cases unsuccessful surgical measures

had been performed prior to the patient's admission. In the fifth case, an operation which I performed for cosmetic purposes was unsuccessful. It seems, therefore, that operation unaccompanied with orthopic procedures is not likely to be successful in these instances and may increase the patient's distress by making diplopia constant. Likewise, glasses and orthoptic procedures seem of little benefit without accurate surgical correction of the deviation. It should be noted, however, that no patient whom I observed was under 8 years of age. Strabismus recognized earlier in childhood might be more amenable to the nonoperative procedures.

SUMMARY

Seven cases of esotropia are reported as possible examples of a clinical entity in which the squinting eye is so deviated that its physiologic blindspot plays a special role as a central scotoma. The history is that of a mild degree of convergent strabismus with periodic diplopia. The syndrome consists of hypermetropia or anisometropia, esotropia of 12 to 17 degrees for distance fixation, normal retinal correspondence and a binocular visual field in which the physiologic blindspot of the squinting eye constantly overlies the point of fixation. Fusional ability, with a limited amplitude of convergence and divergence, can be demonstrated by haploscopic devices adjusted to the deviation of the eyes.

The prognosis for restoration of comfortable single binocular vision is excellent if this "blindspot syndrome" is recognized and treatment is properly directed. In addition to glasses and surgical measures, orthoptic training must be utilized to develop an adequate amplitude of fusional movements and to establish a proper convergence-accommodation mechanism, otherwise, postoperative diplopia is annoying, and there is a tendency for the eyes to return to the squinting position.

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DERMATOMYOSITIS WITH RETINOPATHY

Report of a Case

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DERMATOMYOSITIS is a rare disease of protean manifestations. It is characterized clinically by degeneration of many of the muscles of the body together with a nonsuppurative inflammation and atrophy of the skin and mucous membranes. Involvement of the retina is the rarest manifestation of this rare syndrome. The retinal involvement was first noted by Bruce¹ in 1938 in a report of 3 cases, in 1 of which autopsy was performed, with histologic examination of the posterior segment of the eye. The case to be reported represents a second one in which histologic examination of the eye at autopsy was possible.

CLINICAL FEATURES

The disease was first described in 1863 by Wagner². It may appear acutely, with severe and rapidly progressive symptoms, or it may be seen in a subacute or chronic form, with remissions and exacerbations and sometimes complete recovery. In 2 of the 3 cases reported by Bruce¹ the patient recovered, and there was complete absorption of the retinal lesions. The chronic form is usually insidious in onset, with fever of low degree, malaise, anorexia, loss of weight and weakness. A rash is usually associated at some stage and is variable. The most characteristic cutaneous lesion is patchy erythema, which is faintly indurated, slightly scaly and dry. Keil³ noted a characteristic facies composed of two elements (1) definitely swollen eyelids with some swelling of the adjacent portion of the cheeks and nose, and (2) a background of faint rosy or pale blue skin.

The net effect of these appearances is to create a sort of heliotropic bloating of the face, resembling the early stages of cadaveric decomposition.

From the Neurological Service of Dr Nathan Savitsky, Morrisania City Hospital.

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Nov 1945.

1 Bruce, G M. Retinitis in Dermatomyositis, *Tr Am Ophth Soc* **36** 282-297, 1938.

2 Wagner, E. Fall einer seltenen Muskelkrankheit, *Arch f Heilk* **4** 282, 1863.

3 Keil, H. Manifestations in Skin and Mucous Membranes in Dermatomyositis, with Special Reference to Differential Diagnosis from Systemic Lupus Erythematosus, *Ann Int Med* **16** 828-871 (May) 1942.

The mortality rate is 50 per cent. Calcinosis universalis sometimes occurs, with deposition of calcium in the subcutaneous tissues, muscles and joints. The outcome when recovery occurs is likely to be marked by residual muscular atrophy and permanent cutaneous changes. The muscles of the shoulder girdle, arms and legs are particularly susceptible. O'Leary and Waisman⁴ noted that the distal musculature of the extremities suffers less than the proximal. The muscles are characteristically painful and tender to the touch. Muscular atrophy occurs, and the disease is frequently associated with muscular contractions and fixed joints. The mucous membranes of the mouth and the conjunctiva frequently share in the nonsuppurative inflammation that involves the skin. Depending on the degree of muscular involvement, the symptoms are referable to many of the body systems, weakness of the trunk and the extremities, as well as hoarseness and dysphagia, are seen. Involvement of the diaphragm and intercostal muscles produces dyspnea, bronchopneumonia and respiratory paralysis are the usual causes of death. Erysipelas may develop, with overwhelming toxicity and death. Cardiac failure may be caused by involvement of the heart muscle, electrocardiographic abnormalities are frequent. Sphincteric weakness is found. Subcutaneous edema is a common finding and may be firm or pitting. The distribution of the cutaneous manifestations is not determined by the extent of muscular involvement. Mild pigmentary and atrophic changes of skin may be seen over the joints.

Dermatomyositis may involve the eyes in many ways.

Eyelids—In the average case the eyelids represent the first tissues to be involved, and the appearance exhibited by the lids is of cardinal importance. Involvement of the lids may be the only cutaneous sign. As a rule the lids are swollen and pink. Careful examination will reveal that the rosy hue is due to the presence of numerous, closely set telangiectases. The edematous area of infiltration will generally pit on pressure and is very loose, the lower lids may hang in folds. In some cases the edema is firm. The lids may be tender to the touch, owing to involvement of the orbicularis oculi. The edema of the lids in this disease is differentiated from that due to glomerulonephritis by the presence of telangiectases and the absence of renal involvement. The association of edema of the lids and muscular pains gave rise to the old name of pseudo trichinosis, the differentiation from true trichinosis is made by the presence of the inflammatory reaction, i. e., the erythema, telangiectasia and pigmentation. Subconjunctival hemorrhage, which is likely to occur in trichinosis, is not seen in dermatomyositis. The edema of the lids is differentiated from that of angioneurotic edema by the

⁴ O'Leary, P. A., and Waisman, M. Dermatomyositis, Arch. Dermat. & Syph. **41** 1001-1019 (June) 1940.

transitory nature and the lack of inflammatory reaction in the latter. The telangiectasia is best seen by spreading the lids and rendering them taut, for the small telangiectatic patches may be obscured by the overhanging folds. The edema of the lids associated with sinusitis has its maximum intensity close to the root of the nose. In the later stages of the disease a reticulated pigmentation and superficial localized atrophy replace the edema.

Conjunctiva—The conjunctiva is not so frequently involved as the mucous membranes of the mouth and pharynx. The conjunctiva may be hyperemic, corresponding to the telangiectasia of the skin. This sometimes gives a bluish red color to the palpebral portion. Paralysis of the extraocular muscles due to local muscular involvement has been reported, and diplopia is a rare symptom. Varying degrees of ptosis, strabismus, iritis, nystagmus and exophthalmos have been reported as well. The presence of retinal hemorrhages and exudates was first noted by Bruce¹, the clinical picture and the histologic changes seen in the retina in his cases are similar to those in the case to be reported.

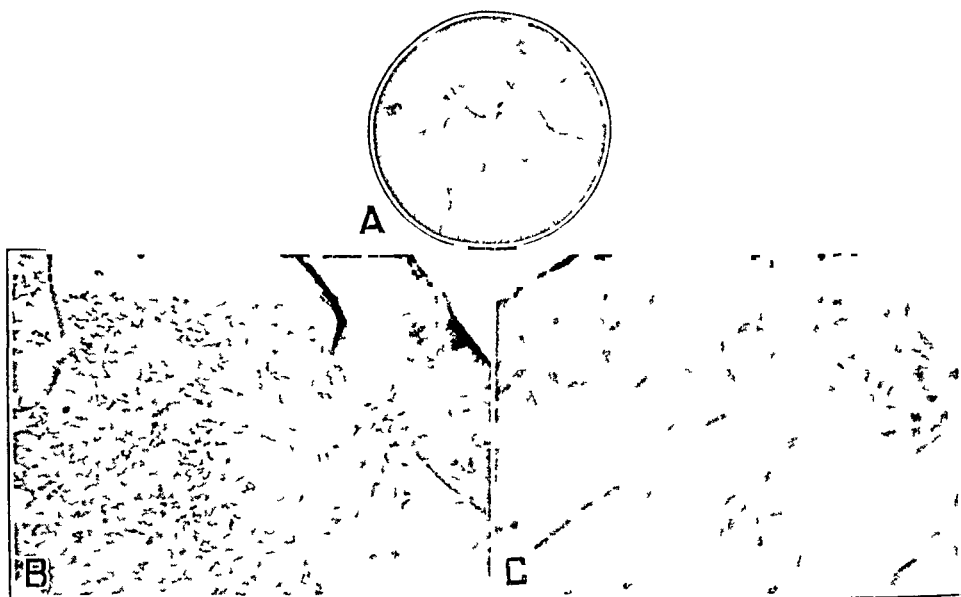
REPORT OF CASE

History,—S. W., a white man aged 53, was observed for the first time on Jan. 28, 1941, on his admission to the neurologic service of the Morrisania City Hospital. The main complaint was generalized weakness, of six months' duration. This had been steady and progressive, and by the time the patient had come under observation at this hospital he was barely able to sit or stand erect unaided. There had been a loss of weight of 20 pounds (9.1 Kg.) since the onset of weakness. Two months prior to his admission the eyelids had begun to swell, and the swelling had persisted. There had been increasing stiffness of all joints of the body with severe pain on extension, especially at the elbows and fingers. The voice had become progressively lower in pitch. There was considerable difficulty in swallowing. A cough, productive of a moderate amount of sputum, had been present for the week preceding admission. There had been one episode of hemoptysis. A rash had appeared over the face in the butterfly distribution, as well as over the shoulders and the tips of the fingers.

Examination—Examination on his admission to the hospital revealed an emaciated man, with a pinched, painful facies. The patient was alert, oriented and cooperative. He preferred to lie quietly in bed in a position of generalized semiflexion and was able to sit erect only when aided. Forced extension at the elbows or knees resulted in great pain. The muscles of the trunk and extremities were extremely tender, lying prone or supine was equally painful. There was a disseminated cutaneous rash in various stages of atrophy. A deep subcutaneous inflammatory reaction was present over the palmar surface of all the fingers, with several patchy areas of necrosis. The inflammation was limited to the palmar surface only. Decubitus ulcers were present over the hips, shoulders, elbows and heels. An erythematous, atrophic eruption was present on the face in butterfly distribution. An erythematous, scaly eruption was present over the entire back. The eyelids were moderately edematous and did not pit on pressure. A few small telangiectases were present in one upper lid. The biceps were small, tense and fibrous to the touch. There were generalized weakness and muscular

atrophy. Fibrillary twitchings of the tongue were seen. There were no focal neurologic signs. Examination of the chest revealed no signs of a pathologic process in the lungs. There were no evident clinical cardiac abnormalities.

Ophthalmic Examination—Examination of the fundi revealed numerous areas of retinal exudate reminiscent of cotton wool patches (figure, A). These areas were at the posterior pole and surrounded the disk and macula. They varied in size from small dots to areas as large as the disk. The color was grayish yellow with a rather dull surface. They were not well circumscribed and tended to fade out into normal retina. For the most part they overlay the vessels, but occasionally they were deep. They were roughly circular and tended to coalesce. Numerous hemorrhages were seen intermingled with the exudate, these were of both the deep round and the superficial striate varieties. The retinal picture was not at all static, and new hemorrhages and exudates appeared as others were absorbed during the short interval that the patient was under observation. The disk and the vessels were normal.



A, artist's conception of the fundus picture, B, histologic section of skin, showing the cellular infiltration in the corium and collagen deposited, C, histologic section of pectoral muscle, showing increased cellularity, fragmentation of muscle fibers and loss of striation.

Laboratory Data—The Wassermann and Kahn reactions of the blood were negative. The urea nitrogen content of the blood was 20 mg per hundred cubic centimeters. The total serum protein was 4.99 mg per hundred cubic centimeters, with an albumin globulin ratio of 1.41. The nonprotein nitrogen measured 38.8 mg. Sugar tolerance studies revealed a normal curve. There were no urinary abnormalities. The electrocardiogram revealed low voltage in all leads, with the T waves depressed in all leads.

Course of Illness—The patient had a low grade fever, with a temperature between 100 and 101 F, until the tenth day of his stay in the hospital, when his temperature rose to 104 F. Facial erysipelas appeared as well as bronchopneumonia. The course was progressively downhill, and he died on the twelfth day after admission.

Autopsy—Autopsy was performed within a few hours after death. Death was reported as due to bilateral bronchopneumonia and streptococcic cellulitis of the face, scalp and mediastinum. The brain showed evidence of slight toxic encephalopathy. Microscopic sections of skin showed thinning of all the layers with dyskeratosis (figure, *B*). The rete pegs were prolonged into the corium. In the latter there was pronounced degeneration of the fibers with collagenous deposits, localized areas of necrosis were present, with an exudate of polymorphonuclear cells and increased vascularity (figure, *C*). The degenerative process and collagen deposits extended into the subcutaneous fat. Histologic examination of muscle revealed an exudate between the muscle bundles, infiltrating and destroying muscle fibers. The exudate was perivascular for the most part and consisted of lymphocytes and large mononuclear cells. There was some proliferation of connective tissue, with replacement of muscle fibers. The muscle fibers in many areas were fragmented and had lost their striations and stained lightly. The arterioles showed thinning with narrowing of the lumen and occasional thrombus formation. Changes were seen in the muscles of the heart and diaphragm and in the biceps and pectoral muscles. Examination of the sectioned eye, as reported by Dr. C. Perera, showed slight postmortem changes in the retina. There were occasional hyaline or lipid changes in the external plexiform layer, especially around the macula. A few small scattered hemorrhages were seen at various layers of the retina. Except for these changes, the eye was completely normal. The vessels showed no pathologic change.

SUMMARY

The case of dermatomyositis reported here is unusual because of the associated retinopathy. This is the second case of this kind in which histologic studies were made. The pathologic process is not specific for this disease.

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DISCUSSION

DR. CHARLES A. PERERA, New York. There was nothing specific about the retinal lesions, which consisted in deposits in the external layers of the retina. One could not make the diagnosis from the retinal picture alone. However, the changes in the 2 cases, that of Dr. Lisman and that of Dr. Bruce, were similar.

PHARMACOLOGIC ACTION OF SOME OPHTHALMIC DRUGS

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DESPITE the fact that most drugs used in ophthalmology are applied directly to the eye, information about their absorption from the surface of the globe is scanty. Only in the case of some of the latest additions to ophthalmic medicine, the sulfonamide drugs and penicillin, has the problem of absorption from the site of their application been systematically studied.

It might be expected, since the conjunctiva is not, like the intestinal tract, provided with special mechanisms for absorption, that absorption from its surface would be very poor. However, as ophthalmologists have long known, it is a good absorbing surface for many drugs. Satisfactory effects are obtained after the local instillation of miotics, mydriatics, cycloplegics, anti-infectives, anesthetics and others. Macht¹ showed that after apomorphine had been placed on a dog's eye vomiting occurred in a few minutes, indicating exceedingly prompt absorption of that drug from the conjunctival sac into the blood stream.

The general phenomenon of absorption has been the subject of considerable recent investigation, and several factors have been determined which influence the rate of absorption from and penetration through skin and mucous surfaces, and which appear to operate in the case of the eye as well as in other parts of the body. Detailed data concerning these factors have now been accumulated which make it possible for the ophthalmologist to prescribe drugs used locally in the eye in the form in which they are most effectively absorbed. For example, it has been shown that the lower the surface tension, i. e., the greater the surface activity of a solution, the more rapidly drugs contained in it penetrate the conjunctiva.² Thus, a solution of an alkaloid or sulfadiazine can be made to penetrate much more quickly if to its solution a detergent, or wetting agent, is added. Many such surface tension-lowering agents are now known, their production has been stimulated for industrial reasons. They

From the Department of Pharmacology, Cornell University Medical College
Read before the New York Society for Clinical Ophthalmology, Nov. 5, 1945

1 Macht, D. I., and Teagarden, E. J., Jr. The Effect of Light on the Behavior of Rats After Injections of Quinin and Quinidin Sulphates, *J. Pharmacol. & Exper. Therap.* **22**: 21 (Aug.) 1923.

2 Bellows, J. G., and Gutmann, M. Application of Wetting Agents in Ophthalmology, with Particular Reference to Sulfonamide Compounds, *Arch. Ophth.* **30**: 352 (Sept.) 1943.

decrease the interfacial tension between air and liquids and make the contact between solutions and the conjunctival surface more intimate. Dermatologists have been using wetting agents for some time to promote penetration of the skin, but their use in ophthalmology has been more recent. Attention has been called to the fact that many of them are far too toxic for use in medicine. Some of those which can be used on the skin are irritant to the conjunctival surface in even moderate concentration. But when required, effectual concentrations of some of these wetting agents may be used with safety.³

The osmotic tension of solutions also influences the rate of absorption. The closer the approach to isotonicity, the more rapid the absorption. Tables on the tonicity of solutions of various ophthalmic drugs, indicating the amount of salt necessary to add to make them isotonic with tears, are available.⁴ The p_H of solutions is important in modifying the absorption as well as the irritant properties of solutions used on the eye. The closer the approach to the physiologic p_H of about 7.5, the less the conjunctiva is irritated.⁵ Most, but not all, ophthalmic drugs are best absorbed from the conjunctiva when in alkaline solution. Shifting from an acid to an alkaline p_H may increase absorption as much as twenty times in the case of certain drugs. Buffer solutions may be prepared with which one can make solutions of optimal p_H of virtually all ophthalmic drugs. Tables for their preparation have been published.

Ophthalmic prescriptions should, therefore, take into consideration the surface tension, p_H and osmotic tension. It is possible to combine all these factors in a solution compatible with an effective concentration of most drugs so that a nonirritant, well absorbed, pharmacologically active preparation is obtained.

I shall consider here only the anti-infective and the choline group of drugs.

ANTI-INFECTIVE DRUGS

The two new anti-infective drugs, the sulfonamide compounds and penicillin, are so superior to anything before available that there should now also be new and higher standards of antibacterial effectiveness. It is worth while to evaluate the older local antiseptics in the light of such new standards to see whether they still have any place in the treatment of local infections of the eye.

3 Leopold, I. H. Local Toxic Effect of Detergents on Ocular Structures, *Arch Ophth* **34** 99 (Aug.) 1945.

4 Cogan, D. G., and Hirsch, E. O. The Cornea. VII. Permeability to Weak Electrolytes, *Arch Ophth* **32** 276 (Oct.) 1944.

5 Elvin, N. C. The p_H and Tonicity of Ophthalmic Solutions, *Arch Ophth* **29** 273 (Feb.) 1943. Cogan and Hirsch.⁴

An antiseptic is a substance which retards the development of disease-producing bacteria. There are a host of such substances. It is possible to demonstrate many apparently desirable and useful properties of these antiseptic substances in the test tube. Some can be shown to have certain bacterial specificities, while others are polyvalent, some penetrate agar gels well, the potency of others seems not to be disturbed much by the presence of pus, protein or tears, some can be shown not to interfere much with the *in vitro* activity of leukocytes or fibroblasts, and some seem to be potent in exceedingly high dilution. But however strongly such information seems to indicate that a chemical antiseptic is desirable, the best evidence is that *in vitro* information has no bearing on the results which may be obtained *in vivo* or on the usefulness of the drug in the local treatment of infections of the skin and mucous surfaces of the body. The *in vivo* test is the only true test of the effectiveness of a substance.⁶

The body has potent and useful antibacterial properties of its own. It has been shown that chemical antiseptics may interfere with these normal anti-infective actions in the body. Lysozyme is an important natural antibacterial agent in tears. There is evidence adduced by Fleming⁷ long before he discovered penicillin that when lysozyme is mixed with some chemical antiseptics the two may prove to be mutually antagonistic and vitiate promptly each other's antibacterial properties. Such a reaction developing between the lysozyme in tears and a chemical antiseptic instilled in the conjunctival sac therefore strongly favors the development of bacteria. If local irritation should follow the use of the chemical antiseptic, bacterial growth would be still further enhanced.

During World War I, when there were no sulfonamide drugs or penicillin, local antiseptics were freely used in wounds. Many studies even then indicated that the best results were obtained when contaminated wounds were irrigated with sterile saline solution, and not when treated with antiseptic solutions. This fact is now more generally recognized. There is considerable evidence to show that sterile wounds heal far more rapidly when no antiseptics are applied. The indications are that when no infection is present the local use of antiseptics retards healing, and that when infection is present strong chemicals may retard the eradication of the bacteria as well.⁸ The usefulness of local antiseptics is indeed limited in most parts of the body, and I doubt whether the eye is an exception to this rule.

6 Conferences on Therapy. Evaluation of Local Antisepsis, New York State J Med 44 2606 (Dec 1) 1944

7 Fleming, A. Antiseptics and Chemotherapy, Proc Roy Soc Med 33 127 (Jan) 1940

8 Fleming, A. The Action of Chemical and Physiological Antiseptics in a Septic Wound, Brit J Surg 7 99 (July) 1919 Footnote 6

The reason that the sulfonamide drugs seemed so miraculous is that they were the first polyvalent anti-infective agents that did the work which had so long been hoped for from chemical antiseptics. The sulfonamide compounds may be an old story today, but there are still important infections in the treatment of which penicillin is ineffectual and for which the sulfonamide compounds can be used to advantage.

I should like to press the question of the local use of sulfonamide drugs as against their systemic administration in the treatment of infections in the eye. Originally it was thought that local use was desirable, since it would produce high concentrations of the drug at the site of application. An experience has accumulated which has led to the questioning of this hypothesis. Unfavorable results have followed indiscriminate application of sulfonamide drugs directly to the peritoneal sac, as well as to other body cavities and surfaces. In the beginning of World War II, the sulfanilamide powder dispenser was a much used item in the official first-aid field kit, and the contents were freely dropped into field wounds. Before the war was over, by Army directive, these dispensers were removed from the kits, and soldiers wounded on the field were given sulfonamide tablets orally instead. The results following oral administration were far superior to those obtained with local use. The powders, used locally, delayed healing, while bacterial eradication was effective by oral administration.

All evidence indicates that the sulfonamide drug operates from the interior of a cell, and not as a surface-acting material. Its presence inside the cell is important, and systemic administration seems to be the most efficient method of getting the drug there. This has been supported by many observers and is the conclusion of a recent extensive report.⁹ There seems to be little in support of the local use of sulfonamide drugs. With respect to the eye, there is evidence that after systemic administration high concentrations in the globe are achieved, while absorption from the surface is not great. In addition, although all do not agree, some investigators have found that its local use delays healing.¹⁰ Many ophthalmologists continue to use sulfonamide drugs locally for ocular infections, but it might be well for them to examine their results more critically.

Penicillin has taken the limelight in general medicine and an important spot in ophthalmic medicine as well.¹¹ It is absorbed from the surface

9 Meleney, F. L. A Statistical Analysis of a Study of the Prevention of Infection in Soft Part Wounds, Compound Fractures and Burns with Special Reference to the Sulfonamides, *Surg., Gynec. & Obst.* **80** 263 (March) 1945.

10 Bellows, J. G. Local Toxic Effects of Sulfanilamide and Some of Its Derivatives, *Arch. Ophth.* **30** 65 (July) 1943. Leopold, I. H., and Steele, W. H. Influence of Local Application of Sulfonamide Compounds and Their Vehicles on Regeneration of Corneal Epithelium, *ibid.* **33** 463 (June) 1945.

of the eye and when taken systemically finds its way into the globe Penicillin is quickly eliminated from the body Penicillin may be used locally to advantage—it is surface active against bacteria and nonirritant even in high unitage Recently it has been shown that its oral administration is practical About five times as much penicillin must be given by mouth to produce effects equivalent to those of intramuscular administration Thus, 100,000 units taken by mouth is equivalent in effect to 20,000 units given intramuscularly Much has been made of the necessity of neutralizing the acid of the stomach with a buffer when penicillin is administered orally However, the use of a buffer is not essential, and penicillin alone taken by mouth apparently works just as well as the tablets now available, which combine the penicillin with sodium citrate¹² A cheap and simple procedure is to use the contents of the usual parenteral ampule dissolved in tap water

Penicillin treatment should not be terminated until an infection is completely eradicated, or relapse may develop In penicillin therapy a continuously maintained concentration of the drug is most important Peaks of concentration which are followed by low levels serve no useful purpose They represent wasted penicillin It is the highest continuously maintained level which is the effective level, no matter how high the occasional peak

CHOLINE DRUGS

Drugs acting on the autonomic nervous system have long been used in ophthalmology, perhaps longer than in any other branch of medicine A great deal of earlier pharmacologic information about these drugs was obtained through observations made in ophthalmology The choline group of drugs, acting on the parasympathetic system, has only lately entered the field of ophthalmology¹³ Their parasympathomimetic action in the eye simulates that of stimulation of the oculomotor nerve, namely, miosis This effect is produced by oculomotor stimulation, since a choline, acetylcholine, is normally elaborated at the nerve terminal when it is stimulated It is the acetylcholine so produced which causes the miosis In a similar manner, stimulation of the vagus nerve and its bulbar and sacral counterparts produces effects on glands, organs and blood

11 von Sallmann, L, and Meyer, K. Penetration of Penicillin into the Eye, *Arch Ophth* **31** 1 (Jan) 1944 Leopold, I H, and LaMotte, W O, Jr Penetration of Penicillin in Rabbit Eyes with Normal, Inflamed and Abraded Corneas, *ibid* **33** 43 (Jan) 1945 Dunnington, J H, and von Sallmann, L Penicillin Therapy in Ophthalmology, *ibid* **32** 353 (Nov) 1944

12 Bunn, P A, McDermott, W, Hadley, S, and Carter, A The Treatment of Pneumococcal Pneumonia with Orally Administered Penicillin, *J A M A* **129** 320 (Sept 29) 1945

13 Kravitz, D Carbaminoylcholine Chloride in the Treatment of Glaucoma, *Arch Ophth* **32** 283 (Oct) 1944

vessels elsewhere in the body. The acetylcholine so produced is almost instantaneously destroyed in the body by an enzyme called cholinesterase. This destruction prevents acetylcholine from accumulating in the body. When acetylcholine is injected into the body, it produces the same effects as parasympathetic stimulation, as might be expected, since this is what parasympathetic stimulation itself does. The injected acetylcholine is also quickly destroyed by esterase. Its effects are so short lived that acetylcholine is not a clinically useful drug.

The beta-methyl derivative of acetylcholine, mecholyl chloride, is far more slowly destroyed by esterase than is acetylcholine itself. Effects are therefore of longer duration, making mecholyl clinically useful. Another choline, carbaminoylcholine chloride, called Carbachol when prepared for ophthalmic use, is not destroyed by esterase. Therefore, when carbaminoylcholine is introduced into the body, effects of much longer duration than those of mecholyl are obtained. Since it is poorly absorbed, the action of carbaminolcholine, after local instillation in the eye, is considerably enhanced by combination with a wetting agent. For this purpose zephiran chloride is often recommended.

This is only part of the story, however. Physostigmine and neostigmine, which are not choline derivatives, also simulate the effects of parasympathetic stimulation. They achieve this, however, by destroying esterase, so that acetylcholine formed during the normal physiologic tonic stimulation of the parasympathetic system is not destroyed but accumulates until pronounced parasympathetic effects are produced. After the administration of physostigmine or neostigmine, acetylcholine itself if injected produces effects of much longer duration because its destruction by esterase is delayed. The same is true of mecholyl. The reported potentiation of the effects of mecholyl in the eye by neostigmine is due to the inhibition of esterase by neostigmine. The combination of mecholyl and neostigmine produces virtually the same effect as that of carbaminoylcholine alone, since the latter needs no protection against the destruction by esterase.

Cholines can, of course, produce profound and serious systemic effects throughout the body—slowing of the heart, depression of blood pressure, violent peristalsis and intense nausea. However, large doses by mouth produce only minute effects, and parenteral administration is required to produce marked systemic actions. For this reason, there is little danger of systemic poisoning from the swallowing of choline drugs which may drain down through the nasolacrimal duct. However, when the drug is injected directly into the globe, the danger of systemic poisoning from mecholyl or carbaminoylcholine must be considered. Atropine, 1 to 2 mg given intramuscularly or intravenously, is the best antidote and should be kept prepared for instant use.

One new derivative of carbaminoylecholine deserves special mention. This substance, called dibutoline, is a dibutyl derivative of carbaminoylecholine and was recently introduced by Swan and White¹⁴. The simple chemical change increases its surface activity and reduces its surface tension, so that it is well absorbed from the eye. The startling feature, however, is that this derivative of acetylcholine has exactly antagonistic pharmacologic effects to those of carbaminoylecholine, and, instead, behaves like atropine. It is a mydriatic and cycloplegic. Its mydriatic action comes on readily and lasts for nearly twenty-four hours, when it falls off quickly. Its cycloplegic action parallels its mydriatic action, so that mydriasis can be used as a measure of cycloplegia. It appears to be nonirritant and nontoxic by systemic administration in exceedingly large doses. Since it is a detergent in its own right, it shares the antiseptic action which wetting agents possess, as well as their generally good absorption.

It is interesting to speculate why there should be this reversal in effects. Why should a choline act like atropine? The best explanation is that this substance is inactive but that it competes with acetylcholine. The parasympathetic end organs do not distinguish between the two drugs because they are so similar in constitution. When the dibutoline is present, it displaces the normally formed acetylcholine and locks with the effector parasympathetic cells, blocking the tonic action of the acetylcholine. Thus, the sympathetic system is permitted to predominate. Dibutoline does not prevent the formation of acetylcholine, it merely blocks its action. The effect of dibutoline can be enhanced by combining it with epinephrine-like substances or with atropine.

It is certain that dibutoline, when it becomes commercially available, will be used in clinical ophthalmology, and it is probable that it will be used in internal medicine as well.¹⁵

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14 Swan, K. C., and White, N. G. Dibutoline Sulfate. A New Mydriatic and Cycloplegic Drug, *Arch. Ophth.* **33** 16 (Jan.) 1945, Di-N-Butylcarbaminoylecholine Sulfate. A New Cycloplegic and Mydriatic Drug, *ibid.* **31** 289 (April) 1944.

15 Peterson, C. G., and Peterson, D. R. Dibutoline. I. Pharmacodynamic Actions of a Choline Ester with Atropine-like Properties, *J. Pharmacol. & Exper. Therap.* **84** 236 (July) 1945.

STABILITY OF PENICILLIN IN OPHTHALMIC SOLUTIONS

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IN THE past year several reports have been made concerning the stability of penicillin in solution or in ointment mixture. Gots and Glazer¹ found that specimens of solution and ointment containing 1,000 units per cubic centimeter remain active for approximately one month at room temperature. Kirby² found "considerable activity" in an isotonic solution of sodium chloride containing 100 units per cubic centimeter after remaining in an open bottle for five months. Stein,³ using 19,285 units per gram, reported that his ointment retained about 80 per cent of its original strength after five weeks at room temperature in the tropics.

On the other hand Milner⁴ claimed that penicillin retained its potency for only four hours when in solution (500 units per cubic centimeter) and for six hours when in ointment form (100 units per gram). Sugar,⁵ using 2,500 units per gram in a water-soluble jelly base, found that the potency dropped to 80 to 90 units per gram after only fourteen days, indicating a terrific waste of penicillin. In none of these cases is it possible to compare or evaluate the results, inasmuch as not all workers compared them with controls. However, the general impression is left that the earlier reports (and some of the recent ones) erred in categorically denying the stability of such preparations. When all the evidence is weighed, it would appear that penicillin does lose its antibiotic powers fairly rapidly when allowed to remain unused in solution or in ointment form for a short period, but not as rapidly as some observers would have it appear. The last word has not yet been written concerning the chemistry of penicillin, its properties or its stability, but for the present I dare say that the use of "old" penicillin

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1 Gots, J S, and Glazer, A M. Stability and Activity of Penicillin in Solution and in Ointment, *War Med* **7** 168-169 (March) 1945

2 Kirby, M M. Stability of Penicillin Solution at Room and Incubator Temperature, *J A M A* **125** 628-629 (July 1) 1944

3 Stein, S H. Penicillin Ophthalmology Ointment, *Bull U S Army M Dept* **4** 8 (July) 1945

4 Milner, J G. Penicillin in Ophthalmology, *Brit M J* **2** 175-178 (Aug 5) 1944

5 Sugar, H S. Personal communication to the author

is definitely contraindicated for parenteral use. The methods of assay are so varied that no one can be sure of the strength in terms of "unitage" in such solutions. Inasmuch as a bacteriostatic concentration in the blood and tissues must be maintained in order for penicillin therapy to be effective, it is obvious that the use of preparations containing an unknown quantity would give the user a sense of false security, and would probably be worthless in its end results. The determination of "unitage" is not insurmountable, but it is questioned whether any two laboratories could duplicate exactly each other's work in this regard. There are many uncontrollable factors that spring up in any assay study, and at best only an approximate estimate can be made. Factors such as the pH of the medium, the content of the medium and variations in sensitivity of strains, all have influential bearing on assay determinations.

In spite of this pessimistic outlook, it would appear that for the ophthalmologist at least penicillin solutions and ointments could be effectively used in spite of lack of knowledge of their potency. The ophthalmologist is confronted with innumerable external diseases of the eye, which in most cases lend themselves to local treatment. Patients with serious ocular diseases are nearly always hospitalized and receive treatment with penicillin by the tried and proved parenteral and iontophoretic methods. One does not risk the use of "old" penicillin in cases of such conditions as gonococcal conjunctivitis, corneal ulcer, orbital cellulitis. Yet most ocular conditions, though minor, are greatly disabling in industry or otherwise. Topical applications are in order, and an exact unitage is unnecessary. What must be sought for is a fairly stable solution that can be made up in small quantities and can be made readily available in any pharmacy for public use on prescription. This solution should be able to supply the necessary bacteriostatic concentration to the tissues involved and remain potent at ordinary room temperature, varying from that found in Maine to that in Texas. It should not be necessary to use the contents of 1 ampule in the treatment of any single patient.

With these needs in mind, an attempt was made to evaluate several preparations both clinically and in the laboratory. I have been impressed with the fact that usually no more than 10 cc of penicillin solution containing 500 units per cubic centimeter need be used in the treatment of any individual patient.

The preliminary study included the use of several vehicles. Following the suggestion of Bellows,⁶ white ointment U S P containing 500 units per gram of the substance was compared with the stability of penicillin in isotonic solution of sodium chloride. This study was repeated with three different samples of penicillin. A standard loop of each preparation was inoculated on a seeded agar

6 Bellows, J. G. Penicillin Therapy in Ocular Infections, *Am J Ophth* 27:1206-1219 (Nov) 1944.

plate and allowed to incubate for forty-eight hours. This procedure was repeated every fourth day until no zone of inhibition occurred. Similar experiments were performed (repeated three times) using Aquaphor⁷ as the ointment base, containing 500 units per gram. At the same time part of the material was set aside for clinical use in treatment of such conditions as catarrhal conjunctivitis, hordeolum externum and blepharitis. In each case a small portion was placed in the refrigerator to compare with that of the uncooled specimens. This preliminary work was done during the months of January through March, in Texas, and the material was allowed to remain at room temperature, which averaged from 75 to 85 F.

After approximately fourteen days all specimens of ointment showed extreme loss of potency, the greatest loss occurring in the Aquaphor mixtures. Only 1 sample of the white ointment mixture retained a potency of 50 per cent after twenty days, the others losing 60 per cent of their activity after the fourteenth day. It was also noted that the patients found use of the ointment impractical. Few became adept at introducing the ointment into the cul-de-sac with a glass rod or swab. In view of this impracticability, and because of their meager lasting power, the ointments were discarded and other vehicles were sought for. It was found that penicillin (1 ampule dissolved in 2 cc of distilled water) mixed readily in a fine suspension with several of the oils. Cod liver oil and olive oil were chosen for further study.

The method of assay required modification after it was found that the oil tended to disperse unevenly over the surface of the agar, resulting in a variety of bizarre zones of inhibition. The ideal method proved to be that advised by Vincent,⁸ with some modifications. A circular disk of heavy filter paper, 2 cm in diameter, was saturated with 0.10 cc of the penicillin-oil suspension and placed in the center of the seeded agar plate. Clearcut zones of inhibition resulted. This method (to be described fully) was then used for all subsequent examinations. It was found that the cod liver oil suspension retained approximately the same bacteriostatic power as did the ointments after being left unrefrigerated, at room temperature, for fourteen days. A 50 to 60 per cent loss of potency in that period still seemed to represent a terrific waste of penicillin, although clinically the results were good. However, the clinical result was quite expected, in view of the low concentration of penicillin that is necessary to inhibit the susceptible organisms.

The results with the olive oil-penicillin suspension were better. At the end of fourteen days (on the basis of measurements of the zones

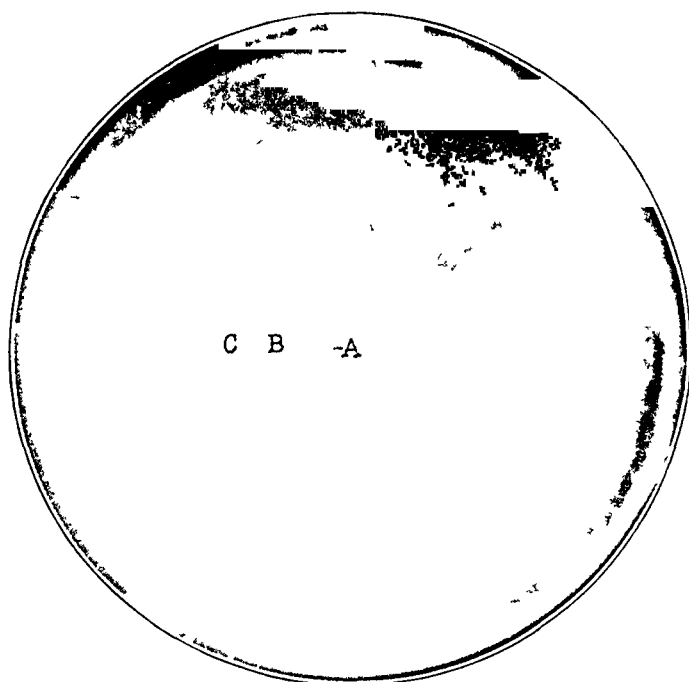
⁷ Aquaphor (Dulse Laboratories, Inc.) is a base containing 6 per cent of a group of esters of cholesterol (chiefly oxycholesterol) in an aliphatic hydrocarbon (petrolatum) base.

⁸ Vincent, J. G., and Vincent, H. W. Filter Paper Disc Modification of Oxford Cup Penicillin Determination, *Proc. Soc. Exper. Biol. & Med.* **55** 162-164 (March) 1944.

of inhibition) the mixture retained 85 per cent of its original strength. At the end of twenty-one days the suspension had 65 per cent of its potency. Further change of potency occurred as shown in the accompanying tabulation.

Interval, Days	Percentage
28	45
35	40
42	36
55	14
70	11

As stated previously, the penicillin mixed readily with the oil in a fine suspension. The naked eye could not detect that the mixture was not actually a solution. Ten cubic centimeters of this mixture was prescribed, and the patient was advised to instill drops every two hours with an eye dropper. The oil suspension seemed to be an ideal medium



Culture plate showing the various zones of inhibition surrounding a filter paper disk impregnated with penicillin. *A* indicates the filter paper disk, *B*, the pellucid zone of inhibition, and *C*, the clear zone of inhibition.

in that the tears did not readily wash the material out. The oil infiltrated every crevice and fold of both the upper and the lower fornix and bathed the lid margins with the same oily film. Examination with the slit lamp one hour after instillation revealed that the oily film was still present. The instillation of this mixture was not accompanied with smarting and proved effective in the treatment of acute and chronic conjunctivitis, hordeolum externum and, especially, seborrheic and

ulcerative blepharitis. However, in comparing these results in the treatment of blepharitis with those for sulfathiazole ointment over a period of many months no great difference could be noted. As to the lasting power, it seemed fairly obvious that the olive oil medium was superior to any of the ointment mixtures.

The last experiments dealt with the use of solutions. Previously, while the ointments were being experimented with, comparisons had been made with penicillin in isotonic solution of sodium chloride and in distilled water. Both solutions appeared to retain their potency about as long as did the ointments, i. e., they lost approximately 60 per cent after fourteen days. (The refrigerated samples retained practically all the original strength after four months.) Although Bigger⁹ and others claimed that the antibacterial activity of penicillin is inhibited by human serum or blood, the final experiments involved the use of pooled human blood plasma and normal serum albumin (human). The use of the blood mediums was based on the uniformly good results I have obtained with the use of human blood (either plasma or whole blood) as a topical application in the treatment of corneal abrasions and ulcers. For the past four years this treatment has been under investigation by this author and found to be effective. In view of the avascularity of the cornea, and because many corneal diseases heal concomitantly with neovascularization, it was thought logical to provide blood elements directly to the lesion to assist in the healing process¹⁰. It was thus deemed worthy to combine the blood with penicillin in order to ascertain its synergistic or its antagonistic effects on stability.

METHOD OF EXAMINATION

The contents of 1 ampule of sodium penicillin was dissolved in 200 cc of pooled human blood plasma to make a solution containing 500 units of penicillin per cubic centimeter. To the melted and cooled agar (brain, heart infusion) rabbit blood was added and well mixed and then allowed to solidify in a Petri dish. The agar was previously seeded with 0.1 cc of a broth mixture of staphylococci containing approximately 1,200,000,000 organisms per cubic centimeter. A circular disk of heavy filter paper 2 cm in diameter was saturated with the plasma-penicillin solution. It required 0.10 cc of solution to saturate a disk of the size used. The disk of filter paper was placed in the center of the solidified agar surface. The zone of inhibition surrounding the disk was measured after twenty-four hours of incubation. The plasma-penicillin mixture was allowed to remain in a capped bottle in the room and was tested every five to seven days. Exactly the same procedure was followed using blood serum. The latter was obtained by using a preparation of concentrated normal serum albumin which comes in dry form and is mixed with a buffered diluent accompanying the package. One such

9 Bigger, J. W. Inactivation of Penicillin by Serum, *Lancet* **2** 400-402 (Sept 23) 1944

10 Naide, M. Treatment of Leg Ulcers with Blood and Concentrated Plasma, *Am J M Sc* **205** 489-493 (April) 1943

package contains 25 Gm of normal serum albumin and when diluted makes up 100 cc of the solution

Both the plasma and the serum penicillin mixture were tested three times, using the same brand of sodium penicillin

It is significant that this experimentation took place during the months of April, May, June, July and August Room temperatures during this period varied from 80 to 100 F

The plasma mixture after a few days became turbid and contained flocculent material From a dirty yellowish color, this flocculent material became successively grayish and then greenish The appearance was that of contamination with mold Some of the agar plates also showed contamination with green mold, which had the appearance of *Penicillium notatum* Microscopic examination revealed that the constant con-

*Percentages of Potency Retained Based on Measurements of the Zone of Inhibition **

Interval, Days	Plasma Solution No 1 (500 Units)	Plasma Solution No 2 (1,000 Units)	Serum Solution (5,000 Units)
14	74%	92%	84%
28	65%	80%	79%
42	57%	76%	70%
55	48%	66%	60%
70	40%	62%	49%
84	27%	52%	37%
90	19%	47%	31%
100	Negligible	23%	20%
110	Negligible	Negligible	Negligible

* The zone of inhibition is measured in the fresh sample after twenty four hours of incubation and is construed as indicating 100 per cent potency Percentages are obtained by comparing subsequent measurements with the first one

taminant was *Penicillium* However, no means were available for further classification of this mold All samples of the plasma-penicillin mixture seemed to produce some of this "contaminant"

The serum mixture remained a crystal clear yellow at all times In none of the samples was there any semblance of turbidity

Clinical use was made of both preparations, with the serum mixture as the favorite When the latter was instilled in the cul-de-sac, the patient nearly always commented on the soothing sensation Contact of the penicillin with the tissues was enhanced by the "stickiness" of the serum albumin on drying

CONCLUSIONS

A study was made of the stability of various penicillin mixtures, allowed to remain at room temperature, which varied from 80 to 100 F, in a southern climate Stability of sodium penicillin in isotonic solution of the sodium chloride and in distilled water was compared with the stability of mixtures in white ointment U S P and Aquaphor ointment All preparations tested contained 500 units of penicillin per cubic

centimeter or gram. It was found that the ointments remained potent as long as the solutions (water or solution of sodium chloride) but that the loss was rapid and wasteful. It was found that the use of the ointment forms was impractical from the patient's viewpoint, or is at least until such time as the ointment is made available in a collapsible ophthalmic tube. It is doubted whether the two ointments tested here can be used efficiently because their lasting power was not in any way remarkable. It is true, of course, that if greater concentrations of penicillin are used the effectiveness would be proportionately prolonged.

The stability of sodium penicillin in suspensions with cod liver oil and olive oil was compared with that of the drug in ointment and solution form. These suspensions proved more effective than either the ointments or the saline solutions, and the olive oil mixture was the more effective. After seventy days the mixture contained approximately 50 units per cubic centimeter. Inasmuch as penicillin is bacteriostatic for staphylococci in a concentration of only 0.08 unit per cubic centimeter, this old mixture can be said to be still "effective," if not efficient. It is believed that these suspensions need to be further studied and that these oils might in the future become ideal vehicles for sodium penicillin.

The stability of sodium penicillin in blood plasma and in human serum was studied and compared with the stability of the drug in other preparations. It would appear from this study that of all the mixtures tested these solutions gave the best results. This view is strengthened by the fact that room temperatures were approximately 20° F. higher during this portion of the investigation. It would appear that the presence of blood plasma enhanced the action of the penicillin rather than inhibited it. Of the two, the plasma solution appeared to be the more effective and the more stable. A solution containing 500 units per cubic centimeter often equaled in effect some of the preparations containing 1,000 units per cubic centimeter. It is believed that the increased stability of the penicillin-plasma solution might be due to spontaneous production of penicillin. Further study with this solution is indicated. The serum-penicillin solution, while not so effective as the plasma solution, nevertheless proved better than any of the ointments, oils or solutions.

The penicillin-serum solution was chosen for use at this institution because of its more consistent stability and its lack of turbidity and mold growth. The procedure at this hospital is to make up 1 ampule of sodium penicillin in solution of blood serum and dispense the material in 10 cc. quantities through the pharmacy on prescription. Although the 200 cc. that is made up at one time is dispensed within one week, the stock bottle is kept in the pharmacy refrigerator, so that each patient receives the full strength when starting treatment.

In general, clinical results have been good with all the penicillin mixtures when used in the treatment of properly selected patients and when applied frequently, in order to maintain contact with the tissues. Instillation every two hours is advisable as the minimum, and perhaps instillation every hour would be better.

It is believed that the most stable penicillin solution has not yet been discovered, but the variability of the many mixtures tested indicates that a step is being made in the proper direction. At this stage it is my opinion that penicillin solution as used here compares favorably in stability with many of the popular ophthalmic remedies, such as solutions of mild protein silver and physostigmine. The latter solutions are known not to remain "potent" nearly as long as does the penicillin solution and yet are in great repute.

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MARGINAL MYOTOMY

Analysis of Twenty-Two Cases

GLEN GREGORY GIBSON, M D

PHILADELPHIA

OPHTHALMOLOGISTS are in agreement about the value of careful refraction and full optical treatment in the management of concomitant strabismus. Beyond this, however, particularly in the field of surgery, one finds many schools of thought concerning the proper procedure in cases of this disorder. This is not surprising, however, since the etiology and pathology of strabismus remain partly unsettled. However, in spite of these and many other difficulties, gratifying progress in the correction of strabismus is being made. Nevertheless, the frequent occurrence of such undesirable conditions as amblyopia ex anopsia, subnormal binocular vision, incomplete corrections and postoperative overcorrection leaves much to be desired in the treatment of strabismus. In an attempt to decrease the incidence of these undesirable conditions, I have resorted to the use of marginal myotomy of the internal rectus muscles in some carefully selected cases during the past five years. Several similar operations and various modifications of this procedure are used by many ophthalmic surgeons, and no attempt is made in this paper to give credit to those who developed these various procedures. The idea of making the incisions well back in the belly of the muscle was advocated by Chavasse¹ in 1934, and my patients were selected and operated on in essentially the same manner as he described. This operation differs from a partial tenotomy in that it is performed posterior to the tendon, in the muscle, and consequently produces a much greater effect. Because of the careful selection, the number of patients in this series is necessarily small, but the material is adequate to demonstrate that this operation, like so many other surgical procedures, has desirable as well as undesirable features.

The simplicity of the operation and its safe applicability to young patients make this procedure a useful addition to one's surgical armamentarium. The operation consists in two vertical incisions in each internal rectus muscle. The two incisions are placed in the margins of the muscle directly opposite each other, in such a manner that they do not meet in the center, so as to leave a central band of intact muscle (fig 1).

Read at the Eighty-First Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., Nov. 13, 1945.

1 Chavasse, B. *Tr. Ophth. Soc. U. Kingdom* 54:506, 1934, *Worth's Squint or the Binocular Reflexes and the Treatment of Strabismus*, Philadelphia, P. Blakiston's Son & Co., 1939.

The technic of the operation consists in freely exposing the internal rectus muscle. A Prince forceps is placed across the body of the muscle, at right angles to the muscle fibers, as far posterior to the tendon as possible. The two incisions are made close to and parallel with the blades of the Prince forceps directly opposite each other so as to cut all but the central 2 to 3 mm of muscle. The amount of muscle which is left might seem inadequate but actually is not, as neither the rotational nor the convergence function of the internal rectus muscle was impaired. The incisions are made in a series of small snips so that the two incisions will be of equal length, in order that the remaining fibers will be in the center of the muscle. Each incision is about 3 mm in length. No sutures are placed in the muscle, and the conjunctiva is closed. Hemorrhage is more profuse than in other muscle operations.

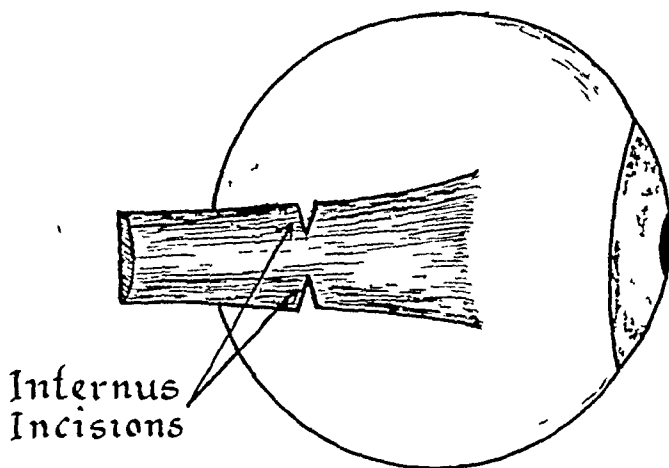


Fig 1—Diagrammatic illustration of the two incisions situated well back in the body of the rectus internus muscle

The object of the marginal myotomy is to decrease the action of a hyperactive muscle. The operation was used in cases in which bilateral recession of the internal rectus was thought to be too extensive a procedure. After this operation the hyperaction of these muscles is no longer manifest and the eyes usually become straightened immediately. Since in most cases this operation was performed at an age before amblyopia ex anopsia had become permanently established, it was hoped that the patients would acquire normal binocular vision and that the eyes would remain straight. Actually, this ideal result of normal vision in each eye, normal binocular vision, and relief from strabismus was achieved in only 6 of the 22 cases representing our series to date.

From the standpoint of this operation, cases of strabismus fall into one of three, not too accurately defined, groups, namely suitable cases, unsuitable cases and cases which may be made suitable by preoperative treatment. The cases which are classified as suitable are those in which

the strabismus is of short duration and the amount not too great and cases in which the strabismus is of the early alternating and symmetric type, particularly if the refractive error is relatively low. Cases which fall in the unsuitable group are those in which the strabismus is of higher degree and of longer duration, cases of profound monocular squint, cases in which the subject is past 7 or 8 years and all cases of divergent strabismus. The cases which may be made suitable for this operation are those in which the patient is under 6 years of age and the strabismus, with the use of glasses or occlusion can be converted into an alternating type. The group of cases which is hereby classified as suitable for this operation is open to the objection that in some of them the condition may be corrected by a nonsurgical method. While this objection may be partly justified, it is not entirely sound, since in waiting the time may come when it is too late to obtain normal binocular vision.

The cases which can be made suitable for operation are those in which total and complete alternating occlusion is used until the strabismus becomes freely alternating. The purpose of this alternation is to develop the monocular retinal function to a point where it is equal to that of its fellow eye, in order that the eyes may be of equal assistance in maintaining parallelism after they have been straightened by operation. If this preoperative precaution is not taken, the chances of obtaining a satisfactory result with this operation are rather remote.

ANALYSIS OF CASES

The material for this report consisted of 22 patients with convergent strabismus who were operated on at Temple University Hospital and have been followed from one to four years after the operation. All but 5 of these patients were under 6 years of age at the time of operation, the average duration of their strabismus from the onset until the operation was only fourteen months. This shows that an attempt was made to use this procedure in cases in which the strabismus was of relatively short duration. The age of onset of strabismus was 2 years or younger in 15 of these patients, indicating that the procedure was not frequently used in cases of typical accommodative strabismus, the onset of which usually occurs at about 3 years of age. Full correction glasses had been worn by 20 of the 22 patients for at least six months prior to operation. If no improvement in the angle of deviation was demonstrable after about six months of the optical treatment, further reliance on this type of treatment was usually discontinued. The refractive errors in the two eyes were essentially equal with respect to the amount of hyperopia or astigmatism in 20 of the 22 cases, indicating that an attempt was made to subject patients with symmetric strabismus to this procedure. There were 2 patients with slight anisometropia in the group. In 10 of the patients the refractive error was less than 2 D of hyperopia, and in only 3 patients was the refractive error higher than 4 D of hyperopia. There were no cases of myopia in this series.

Further evidence of the symmetry of the strabismus in the selected cases was available in the ocular rotations. Eighteen of the patients were recorded as having equal amounts of excessive action of both rectus internus muscles. No patients were included who showed a definite unilateral preponderance of abnormal

rotation in one eye as compared with that in the fellow eye. Patients with typical monocular strabismus were subjected to different types of surgical procedures. Likewise, patients who had high degrees of strabismus or patients with long-standing strabismus were subjected to more extensive types of operation.

Nineteen of the patients had 30 degrees of strabismus or less, and in a number of these patients the strabismus was variable in amount. That is, since many of the patients had strabismus of relatively short duration, the degree of strabismus had not become established at a constant figure at the time of operation. Six of the patients had partial amblyopia ex anopsia which was not completely overcome by what was considered an adequate period of occlusion.

Twenty-one of the 22 patients had a bilateral marginal myotomy. In the 1 patient a unilateral marginal myotomy was performed. The operation takes little time, is easily performed and requires only a few days of hospitalization. There were no complications in the series, and only 1 patient had to have a second operation. There was only 1 instance of postoperative divergence in the series, and in that case the complication was overcome in a few months, without further treatment.



Fig 2—Preoperative and postoperative photographs of a patient who had binocular vision after operation and whose eyes remained straight.

An illustrative case is that of D. C. (fig 2), aged 2 years 9 months, whose mother stated that for the past month the right eye had turned in, at first intermittently and later constantly. The right eye had 10 degrees of convergence, which increased considerably when the eyes were forcibly converged. Fixation was accurate with each eye. The rotation showed a 1 plus overaction of the right rectus internus. On refraction, she was found to have 1.50 D of hyperopia in each eye. Occlusion was ordered, and in three days the left eye became convergent and the right one was straight. One month later she presented the picture of typical alternating concomitant convergent strabismus. The strabismus was 15 degrees, and +1.50 D spheres were ordered. After three days of wearing the glasses the eyes became straight. The eyes remained straight for about a month, when the convergent strabismus again became manifest at 20 degrees with the glasses on. Atropinization and occlusion were again ordered to maintain alternation. Five months after the first visit the strabismus had become 30 degrees, and the action of both rectus internus muscles was 2 plus. Seven months from the time the patient was first seen a bilateral marginal myotomy was performed. The eyes were straight on the first postoperative day and have remained straight for five years. Six weeks after operation she had fusion, and at the present time she has normal binocular vision, the only residual evidence of her strabismus is the slight conjunctival scars.

Figure 3 illustrates the preoperative distribution of strabismus in the 22 patients

The immediate results were gratifying, as 20 of the patients were recorded as having straight eyes at the time of their first visit after hospitalization (fig 4). Almost all the patients had normal rotations

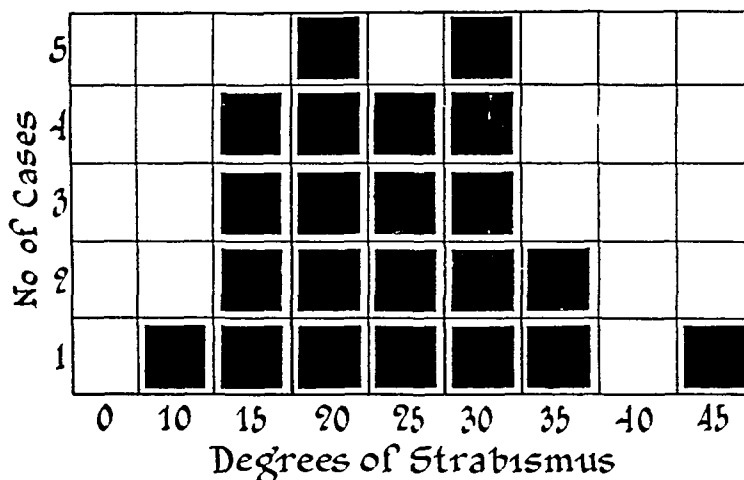


Fig 3—Graphic representation of the degree of preoperative strabismus in each of the 22 cases studied

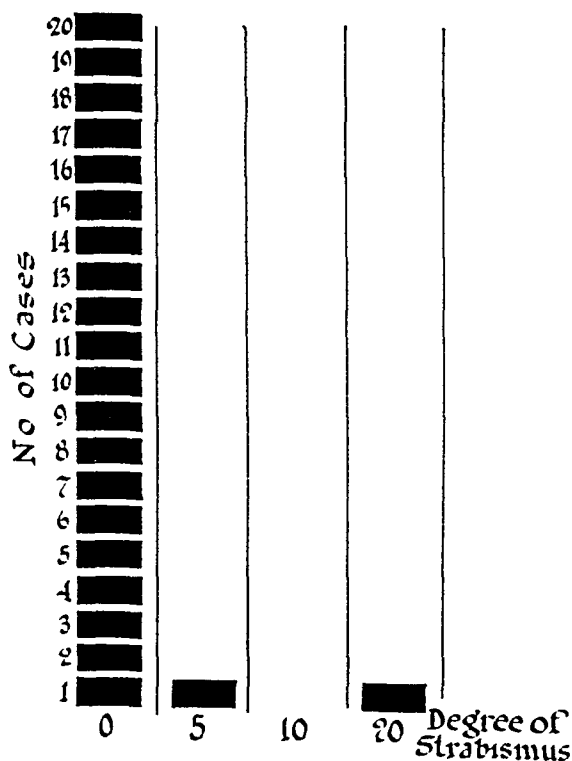


Fig 4—Immediate postoperative result, illustrating the notable improvement in the series

after the operation. The overaction of the rectus internus muscles was almost uniformly relieved, and there was no case of subnormal rotation of the eyeball in the field of the muscle operated on. None of the patients had demonstrable fusion at the first postoperative visit. Two of the patients attained fusion in about three months after the operation.

and 4 in about one year. The method gave good results in 2 patients whose eyes were straight when wearing glasses but converged freely without glasses. In these patients the eyes remained straight without glasses after the operation. When the records were reviewed, at periods varying from one to four years after operation, it was found that the eyes of only 8 of the patients remained perfectly straight and that 12 were found to have from 5 to 10 degrees of residual or recurrent strabismus (fig 5). While this amount of recurrent strabismus was disappointing from the standpoint of the patient's acquiring normal binocular vision, it is consistent with the teaching of Bielschowsky,² who stated that "a small deviation of 5 degrees must be left, particularly if the patients are young children, since a spontaneous decrease in convergence is to be expected." The amount of strabismus which was present in the patients who had recurrences was always considerably less than the

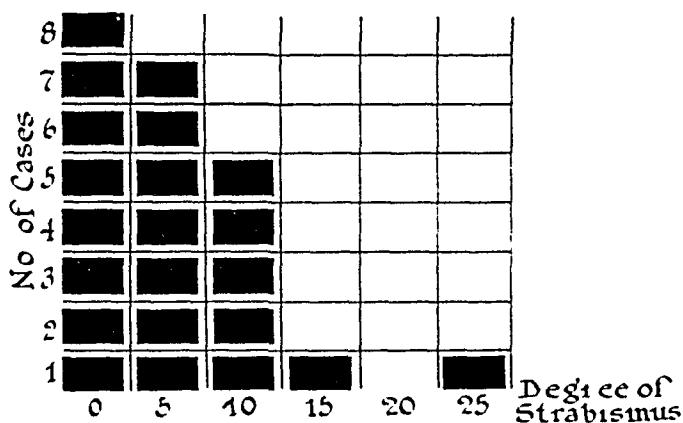


Fig 5—Late postoperative results (one to four years), illustrating the tendency to recurrence

amount which they originally had, as can be seen by comparing figures 2 and 4. Several of the patients had their eyes straight for two to three years after the operation, before the strabismus recurred. It would seem that the incidence of recurrence after operation is too high, particularly in view of the fact that most of the cases were favorable.

A case which illustrates the tendency to recurrence is that of C H (fig 6) aged 2 years 9 months, who had had 12 degrees of concomitant convergent strabismus for two months when first examined. The rectus internus muscles were recorded as being equally hyperactive. The refractive error was corrected with a +1.00 D sphere combined with a +0.50 D cylinder for each eye. The fixation was accurate and equal in the two eyes. Six months later, the left eye turned more than the right and occlusion was ordered. After two months of alternate occlusion, his eyes were freely alternating, and a bilateral marginal myotomy was performed. On the first postoperative visit, the eyes were straight and the rotations were normal. Three months later the left eye turned in 8 degrees at various times. He had no fusion, and occlusion was again resorted to, at the age of 5, because the left eye had become amblyopic. Two years after the operation the eyes turned in 10 degrees without

glasses and 8 degrees with them. The vision was equal in each eye. No fusion was demonstrable.

In considering the possible reasons for recurrences in this series of patients, it would seem that amblyopia ex anopsia was the most apparent single cause. Five of the 6 patients with amblyopia had permanent recurrence of strabismus, and the sixth patient had a recurrence which lasted over a year before the eye became straight. In 2 of the patients the recurrence might possibly be explained by the strabismus being of too long a duration. Two of the recurrences were attributed to the refractive error being relatively too high. One recurrence was attributed to the amount of strabismus, of 45 degrees, being too much to be overcome by this operation. In 3 of the patients no obvious cause for the recurrence was found. One gets the impression from the review of the

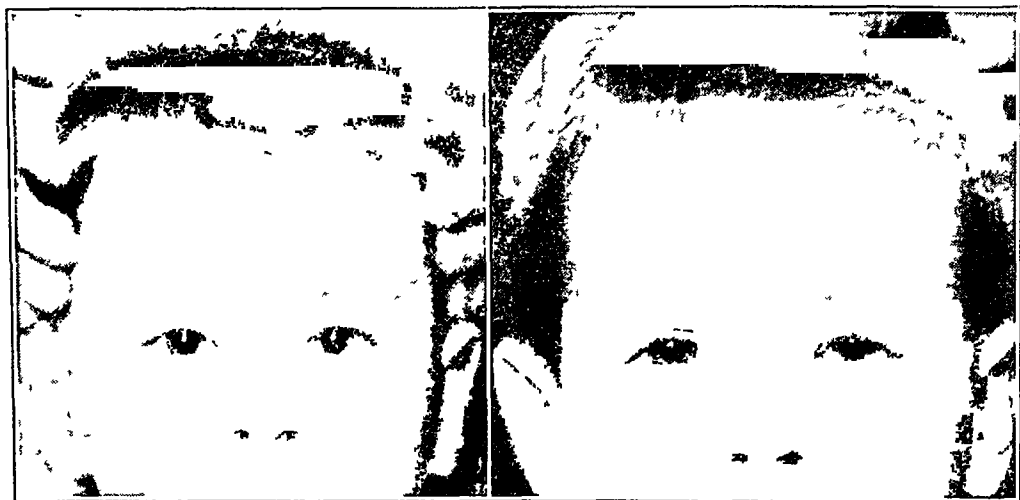


Fig 6—Preoperative and postoperative photographs of patient whose eyes were straightened and who subsequently had a recurrence

cases in which recurrences developed that the important factors which cause failure are defects in the sensory function of the ocular mechanism, rather than the motor abnormalities. The operation was very successful in overcoming the hyperactive rotations even in cases in which recurrence developed. It is possible that more careful attention to the sensory aspects of these cases after operation may have decreased the incidence of residual strabismus in this series. None of the patients had orthoptic treatment.

SUMMARY

The operation of marginal myotomy is useful in certain types of strabismus. It is most helpful in those cases in which bilateral recession might result in a postoperative divergence. In order to avoid the rather high incidence of recurrence, it is necessary to exercise great care in the selection of the cases for this operation.

THE CAPILLARY SPHINCTER IN THE HUMAN RETINA

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STUDIES of the blood vessels of the human retina were primarily stimulated by interest in the anatomy of the structures of the eye-ground as they relate to basic aspects of ophthalmoscopy. The paucity of information to be gathered from the literature on the histology of the retinal vascular system made it necessary to undertake investigations of surface preparations of the choroid and the retina.

A number of these preparations were stained with a great variety of agents before an occasional satisfactory one was obtained. Most of the material was obtained from eyes enucleated for the usual clinical indications. The retinal preparations found most useful were those stained with Weigert's stain for elastic tissue without counterstain. Fixation was with dilute solution of formaldehyde U S P. The best preparations of the choroid were those stained with Mallory's aniline blue. The retina or the choroid was stripped from the underlying layer. In some instances the choroid was bleached. In others this was unnecessary. The tissue was cleared with xylol, stained and mounted on a slide with a cover glass in the usual manner. Those preparations which were selected as satisfactory were more instructive than any previously seen or found reported in the literature. This was demonstrated by the sharply defined details which could be brought out by photomicrography. During the study of these preparations a peculiar abrupt narrowing of certain capillaries was noted where they joined the vessel of the next larger order. This seemed to be a unique discovery, the correct interpretation of which was of the utmost importance.

One had to consider three possibilities, namely that the pinching was (1) an artefact, (2) a pathologic change or (3) the indication of a normal histologic structure.

Though none of these possibilities could be definitely accepted or discarded, the existence of an artefact at that particular place seemed unlikely in the absence of similar changes elsewhere in the capillaries. Higher magnification showed no change at the junction of the capillary and the larger vessel which could be interpreted as pathologic. One therefore had to incline to the view that this narrowing was of a purely histologic nature and that it might be due to a sphincter-like action in

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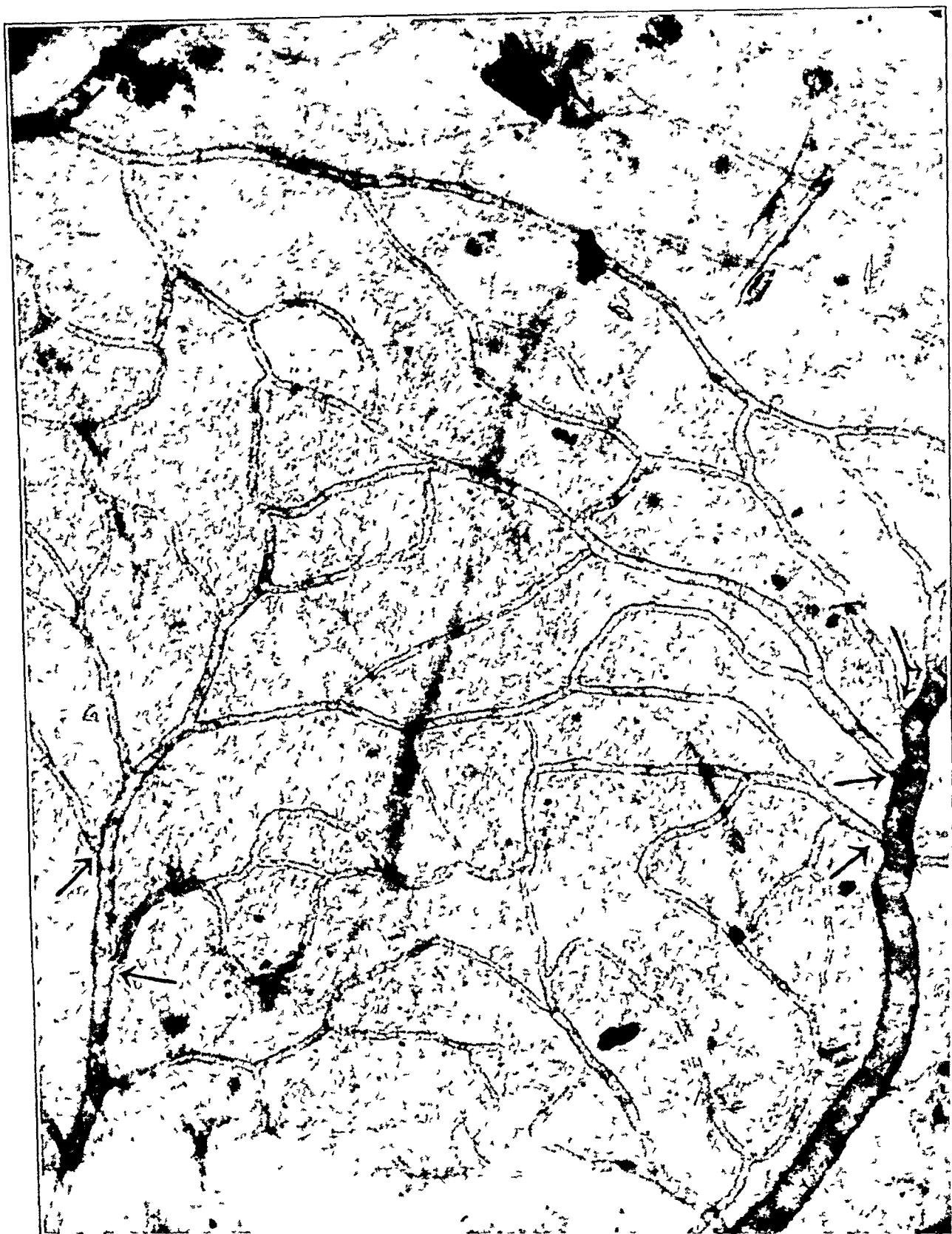


Fig 1—Surface preparation of the entire thickness of the retina, except for the pigment epithelium, from the neighborhood of the equator of the eye. The arrows indicate the constrictions where the capillaries join the vessel of the next larger order.

This photograph and those in the accompanying figures have not been retouched. Weigert's elastic tissue stain without counterstain, magnification, $\times 160$.



Fig 2—One of the regions of junction, showing narrowing. With the immersion lens, a plump, nucleus-like body was seen at the point of each arrow. It was not possible to bring this out in the photograph.

The preparation and staining were the same as those used in figure 1. Magnification, $\times 880$.

this region, because some capillaries did not show this narrowing at the junction with the larger vessel

All the available ophthalmologic literature on retinal vessels was reviewed, without disclosing a similar description. At this point, the work of Chambers and Zweifach¹ and of others² was called to my attention. These investigators, whose contributions are widely recognized, had described a narrowing at the junction identical with that described here which they observed in the capillaries of the bat's wing and of the mesentery of the rat and dog³. Moreover, they had seen the region contract and dilate with sphincter-like effect and had secured satisfactory photographs. Their observations made more reasonable my postulation of the presence of a sphincter-like structure in the capillaries of the retina. Their paper is comprehensive in the field of capillary circulation and should be read in full.

Unfortunately, the living human eye does not lend itself to experiments such as those the anatomists were able to perform on animals. Thus far, the slit lamp has not demonstrated similar junction constrictions in the epibulbar tissues of the human eye. The constriction has not been observed with the ophthalmoscope.

Possible dilatations and constrictions of capillaries by pressure reflected from the larger vessels has long been recognized. A muscle-like constricting effect of the Rouget cells was described by Krough, but his work of late years has been seriously questioned by other authors⁴. Some investigators⁴ expressed the belief that the nuclei of endothelial cells could swell sufficiently to occlude the lumen, thus causing a back pressure which would dilate the capillary.

Figure 3 shows narrowing at the junction of the choroidal vessels. If retinal and choroidal capillary sphincters do exist, their contraction would have a powerful effect on the capillary bed. The sphincters at the junction with the arterioles would decrease the area of the capillary bed, those at the junction with the venules would cause stasis and increase the area of the bed. It is conceivable that a derangement of this sphincter mechanism by disturbance of the sympathetic hormonal relations might be a factor in producing a type of glaucoma simplex.

1 Chambers, R, and Zweifach, B. W. Topography and Function of the Mesenteric Capillary Circulation, *Am J Anat* **75** 173 (Sept) 1944

2 Tannenberg, J. Bau und Funktion der Blutkapillaren, Frankfurt *Ztschr f Path* **34** 1, 1926

3 Tannenberg² is said to have observed precapillary sphincters in fixed preparations of the mammalian eye, but I have been unable to locate the specific article in which he reported this observation.

4 Wiggers, C. J. Physiology in Health and Disease, ed 4, Philadelphia, Lea & Febiger, 1944, p 547



Fig 3—Surface preparation of the choroid, which was stripped from the underlying layer and bleached. Arrows indicate narrowing at the junction of the smaller vessels with those of the next larger order.

Mallory's aniline blue stain for collagen, magnification, $\times 160$



Fig 4—Surface preparation of the retina from an eye removed for absolute glaucoma simplex. There is a dense constriction where dilated capillaries merge with vessels of the next larger order, whereas other capillaries coming off the same larger vessel show no such constriction or aneurysmal dilations. Branches from the dilated vessel seem to have been protected from changes in transmitted pressure, as though their own mechanism was adapted for this purpose. Had a weakness originated in the capillary wall, one might expect that all the capillaries in this region would be similarly affected.

Weigert's elastic tissue stain, magnification, $\times 140$

If this meager evidence is ultimately supported by better substantiated studies, it would seem reasonable to conclude that the retinal capillary aneurysms associated with glaucoma, such as those shown in the surface preparation of the retina (fig 4) from a case of absolute glaucoma simplex, may have had their origin in a prolonged constriction of the sphincter muscle. I have been able to find this picture of capillary aneurysm in some area of the retina of a number of eyes removed in the last stages of glaucoma. The patients from whom these eyes were removed did not have diabetes mellitus. I emphasize this fact in view of the reported⁵ occurrence of capillary aneurysm in cases of diabetes mellitus.

There is perhaps further significance in the fact that Chambers and Zweifach¹ studied the active responses of this region of junction through the application of high dilutions of epinephrine and histamine.

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5 Ballantyne, A. J., and Loewenstein, A. Retinal Micro Aneurysms and Punctate Haemorrhages, *Brit J Ophth* 28 593 (Dec) 1944

REMOVAL OF DEEPLY EMBEDDED FOREIGN BODIES FROM THE CORNEA

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CORNEAL foreign bodies lying close to Descemet's membrane always present a problem. When the eye involved is the patient's only good eye, the necessity for careful surgical handling is proportionately greater. During the past year, 6 deeply embedded corneal foreign bodies requiring removal were seen at this Army ophthalmic center. These foreign bodies were all in eyes with normal vision or with vision correctable to normal. Two of the patients were monocular. A third had only perception of hand movements in the other eye. In a fourth patient the other eye was aphakic, with a corrected vision of 20/70. Two patients had good vision in both eyes.

All the patients were battle casualties, and the foreign bodies were all metallic. Three were found to be magnetic after removal. In this connection, I should like to state, however, that even if the foreign body is magnetic the magnet is useless in removal of these deeply embedded foreign bodies from the cornea until they have been loosened from the surrounding stroma.

REPORT OF CASES

The first case encountered was that of a monocular patient. The foreign body was just below the corneal apex (fig 2, case 1) and was surrounded by a rust stain, which involved the pupillary area. The body was irregular in shape, and examination with the slit lamp showed that it lay in the posterior third of the corneal stroma. The temptation to leave the eye alone was great. However, since the rust stain was obviously spreading and the eye was irritable, it was felt that this could not be done. The following technic was adopted and carried out.

The pupil was widely dilated with atropine. Corneal anesthesia was obtained by instillation of 0.5 per cent tetracaine hydrochloride. With a Ziegler discission knife, a corneal flap was fashioned by means of two incisions meeting at an apex (fig 1a, lines *BA* and *BC*) pointing toward the center of the cornea and containing the foreign body between them. The incisions were beveled toward each other, so as to approach the foreign body more closely (fig 1b). After sufficient depth had been attained, the corneal flap was folded back on its base (fig 1c, line *AC*), and the foreign body was exposed. This was then gently

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freed from the surrounding stroma with the point of the knife and lifted out. The rust stain was carefully curetted away and the corneal flap patted back into place with a spatula. No sutures were necessary. Atropine was instilled and the eye patched. The cornea was completely healed and the patch removed in four days.

In 5 additional cases this technic was subsequently used. The details are given in the following brief case histories.

CASE 1—Pvt R L H was wounded on May 29, 1944 at Veretro, Italy, by fragments of a German mortar shell, sustaining wounds of both eyes, the skull and the right wrist. The left eye was enucleated the same day. When he

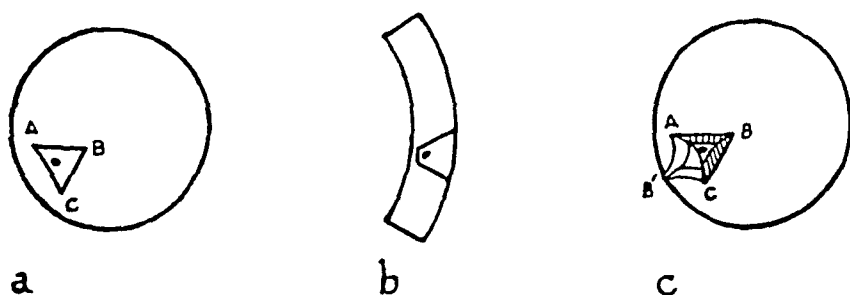


Fig 1—Diagrammatic scheme of corneal flap technic. (a) The cornea is incised along lines BA and BC and not along line AC . (b) The incisions are beveled toward each other. (c) The flap $AB'C$ is then turned back to expose the foreign body. After extraction, the flap is patted back into place with a spatula.

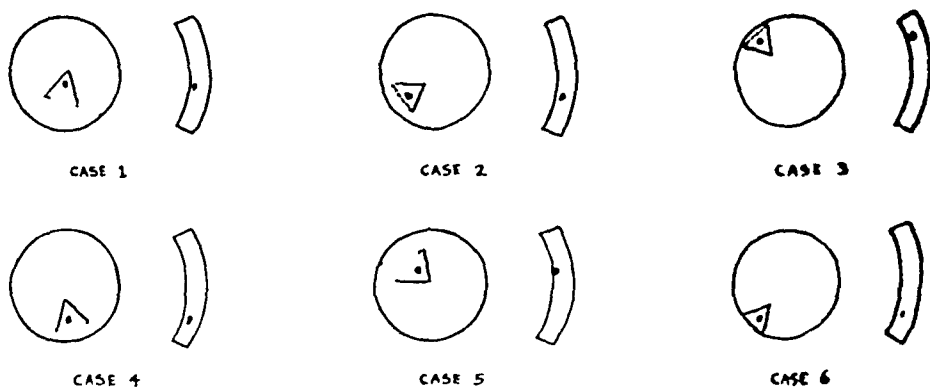


Fig 2—Approximate position of the foreign bodies in each of the 6 cases reported. No attempt has been made to depict the exact size and shape of the corneal foreign bodies.

was admitted to this hospital, vision in the right eye was 20/30, correctable to 20/25. The bulb showed a faint ciliary flush. Examination with the slit lamp disclosed a deeply embedded foreign body just below the corneal apex, which was surrounded by a rust stain (fig 2, case 1). The aqueous showed a faint flare and a few cells. There was a small posterior cortical opacity of the lens at 10 o'clock, and the vitreous showed a few fine stringy opacities. Fundoscopic examination revealed nothing abnormal. On Sept 15, 1944, the

foreign body was removed through a corneal flap, as previously described. Healing was uneventful. On September 18 the cornea no longer stained, and patching was discontinued. The flare persisted, however, and the patient was placed under treatment with atropine and application of hot compresses three times a day. On September 27 the anterior chamber was clear and medication was discontinued. Since plastic surgery of the left lids and socket was required, the patient was under observation until July 3, 1945. At this time the eye was completely white and quiet. A faint corneal nebula still marked the original site of the foreign body. The media and fundus were unchanged. Vision was 20/20, with ability to read Jaeger type 1.

CASE 2—Pfc A M was wounded on July 21, 1944 at Cherbourg, France, by an enemy hand grenade. Fragments entered both his eyes, amputated his right middle finger and lacerated both his thighs. After first-aid treatment, he was evacuated to England, where "fragments of metal were removed from both his eyes." On his admission to this hospital, vision was limited to perception of hand movements at 1 foot (30 cm) in the right eye and was 20/40—1, correctable to 20/25, in the left eye. Both eyes showed multiple corneal maculas. The right eye had traumatic iritis with ragged atrophic iris and posterior synechias. There was also a traumatic cataract. The left eye showed a faint circumcorneal flush and a deeply embedded corneal foreign body (fig 2, case 2). The anterior chamber showed a faint flare. The lens, vitreous and fundus were normal. Treatment for the bilateral iritis was instituted, and both eyes responded well. On Nov 28, 1944 the foreign body in the left cornea was removed through a corneal flap. The cornea was healed on December 2. On December 10 all medication was discontinued. The patient was last seen on Feb 2, 1945, at which time both eyes were white and quiet. Vision was limited to perception of hand movements at 2 feet (60 cm) in the right eye and was 20/25, correctable to 20/20—2, in the left eye.

CASE 3—Cpl G W was wounded near Cherbourg, France, on July 26, 1944 by fragments from an 88 mm enemy shell. He sustained a fractured skull and wounds of the left eye and left foot. He was evacuated to England, where (he stated) a foreign body was removed from his left eye on August 18. On his admission to this hospital, corrected vision was 20/20 in each eye. The right eye was entirely normal. The left eye showed mild iritis with a deeply embedded foreign body in the cornea (fig 2, case 3). On Jan 16, 1945, the foreign body was removed through a corneal flap. On January 19 the cornea was clear and the iritis had subsided. The patient was last seen on May 15, 1945, at which time both eyes were normal and vision was 20/20 in each eye.

CASE 4—Sgt E E L was wounded on Jan 9, 1945, in Belgium by a Teller mine and received multiple wounds of the face, the left hand and the right thigh. On his admission to this hospital, vision was 20/50 in the right eye and 20/40—2 in the left eye. Both eyes showed numerous conjunctival powder burns and superficial corneal opacities. Both anterior chambers were clear, but the irises were irregular and reacted poorly to light. The right cornea showed a deeply embedded foreign body, surrounded by a greenish rust stain (fig 2, case 4). The media and fundi were normal. On April 3 the foreign body was removed through a corneal flap. Patching was discontinued on April 10. On June 28 vision was 20/50 in the right eye and 20/30—2 in the left eye. The reduction in vision was attributed to the corneal opacities.

CASE 5—Pvt E R C was injured in Germany on March 31, 1945 by shell fragments, sustaining wounds of both eyes and the left foot. On his admission to the hospital, vision was 20/25 in the right eye and 20/300, correctable to 20/70, in the left eye. Both eyes showed multiple superficial corneal opacities, with one deeply embedded corneal foreign body in the right eye (fig 2, case 5). There was a slight posterior displacement of Descemet's membrane at this point. There was also mild iritis, but no other pathologic condition. The left eye showed a partial anterior capsular and subcapsular traumatic cataract, which was apparently stationary. On July 10 the corneal foreign body was removed through a corneal flap. On separation of the foreign body from its position, a drop of aqueous slowly formed in the corneal wound. There was no tendency for the iris to prolapse. The corneal flap was patted into position, the eye patched and a supportive bandage applied. The following day the anterior chamber was reformed. Patching was discontinued on July 13, and on July 16 the eye was completely healed and white. On July 23 vision was 20/25 in the right eye and 20/70 in the left eye.

CASE 6—T/5 R D M was wounded by shrapnel in Italy on April 10, 1945, sustaining injuries of both eyes. The left eye had to be enucleated six weeks later. On his admission to the hospital vision in the right eye was 20/25, correctable to 20/20. Examination with the slit lamp revealed a deeply embedded corneal foreign body (fig 2, case 6) near the posterior surface, surrounded by a halo of rust. A faint flare and a few cells were visible in the anterior chamber. On September 20 the foreign body was removed through a corneal flap and the rust stain curetted. The cornea was healed on September 22. On September 27 vision was 20/20 with correction.

COMMENT

It will be noted that in 1 case (case 5) aqueous was lost after removal of the foreign body, which protruded slightly into the anterior chamber. Closure of the corneal flap and supportive dressing resulted in restoration of the anterior chamber in twenty-four hours and uneventful healing, as in the other cases. In all 6 cases the cornea was healed within four days or less. Clean incision of the cornea, instead of "picking" at it, results in less mutilation of corneal stroma, and consequently less corneal opacification. If the cornea should be penetrated, as it was in case 5, the flap is an efficient valve with which the anterior chamber can be sealed off instantly, and it heals in rapidly.

Other precautions are, of course, necessary. One always has to decide what to do with the iris. In cases 1 and 5, in which there was a centrally placed foreign body, the pupil was dilated. In cases 2, 3, 4 and 6, in which the foreign bodies were more peripheral—the pupil was contracted with physostigmine. The purpose was to prevent a prolapse of the iris in case of corneal perforation and sudden loss of aqueous. Experience in case 5, however, showed that loss of aqueous is negligible and that there is no sudden gush outward, as with a keratome incision. Hence it is probable that the iris would

not have prolapsed in any case. This situation is due to the fact that the corneal penetration is minute.

To me, a much more important consideration is loss of the foreign body into the anterior chamber. Fortunately, this did not happen. But no procedure is fool proof, and the possibility must always be kept in mind. Since with this method prolapse of the iris is not a factor, it is probably better to contract the pupil in every case and use the iris as a protective curtain for the lens. Then, in case of accident, the foreign body could be extracted through a keratome incision with forceps or, if magnetic, with a hand magnet, with least danger to the lens.

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NEW MODIFICATION OF THE McREYNOLDS TRANSPLANTATION FOR PTERYGIUM

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DURING the past three years an increasing number of recurring pterygia have been observed in the Army following the classic McReynolds transplantation¹. These failures have also been noted in civilian life. It is the purpose of this paper to offer an explanation for these recurrences and to present a new modification of the McReynolds procedure for their prevention. This method has been employed in 300 cases, with satisfying results.

A brief review of the anatomic framework of the ocular structures involved in the operation for pterygium will prove helpful in the discussion pertaining to the factors which are probably responsible for recurrences.

The subconjunctiva is divided into the superficial and the deep fibrous layer. The superficial layer consists of adenoid tissue, which is loosely arranged. The deep fibrous layer is the one more properly considered the subconjunctival connective tissue layer, rather than a constituent of the conjunctiva itself. It consists of a thick meshwork of collagenous and elastic fibers. Situated below this tissue is Tenon's capsule, that layer immediately surrounding the eyeball in the orbit. This layer thins almost to microscopic thickness as it approaches the limbus. Beneath Tenon's capsule is the episcleral tissue, which consists of a looser structure than the sclera proper, its bundles are more delicate and more tortuous and course in varying directions (Salzmann²). Outwardly, it extends into the loose tissue which fills out Tenon's space. Toward the inner side the bundles are firmer and thicker, and the matting is closer. In this way, the episclera graduates into the tissue of the sclera proper.

For facilitation of discussion, the McReynolds operation will be divided into the corneal and the conjunctival stage. The complete removal of the head of the pterygium, which has infiltrated and destroyed Bowman's membrane and the superficial corneal lamellas, depends on

From the Eye Clinic, Battery General Hospital, Rome, Ga

1 McReynolds, J O. Pterygium Operation, Tr Sect Ophth, A M A, 1924, p 27

2 Salzmann, M. Anatomy and Histology of the Human Eyeball, Chicago, University of Chicago Press, 1912

a painstaking dissection. Not infrequently one observes partial ablation of the head. The neck is grasped and lifted with a fixation forceps, placing the head under moderate traction. The dissection should commence, preferably, at 0.5 to 1 mm beyond the periphery of the infiltrating zone, as observed by slit lamp microscopy. The dissection is brought down to the most superficial layers of the substantia propria and the head completely removed in this plane. This microscopic dissection is accomplished with the aid of a binocular loupe. The magnification thus achieved greatly facilitates the accuracy of the dissection, the aim of which is to render the corneal and limbal sites completely free of residual tissue, so that cauterization will not be necessary. The denuded corneal bed and its edges will occasionally require curettement.

The inherent elasticity of the adhering bulbar conjunctiva along the superior margin of the body and the intrinsic retractility (due to shrinkage of the conjunctiva) of the stretched and tensed pterygium are important factors in disengaging the head from its transplanted site, since it is invariably held insecurely in the subconjunctival tissue.

In the McReynolds operation, the sutures are passed blindly through the loose subconjunctival tissue to emerge from the conjunctiva. The looseness of the subconjunctival tissue does not predispose to firm adhesions with the head of the pterygium. When the black silk sutures are removed on the third to the fifth day after operation, part of the forming adhesion is usually disturbed and broken, and if the retraction pull of the pterygium is sufficiently powerful, it is not long before the neck and the head of the retracted pterygium align themselves in the horizontal meridian to commence invasion of the cornea again.

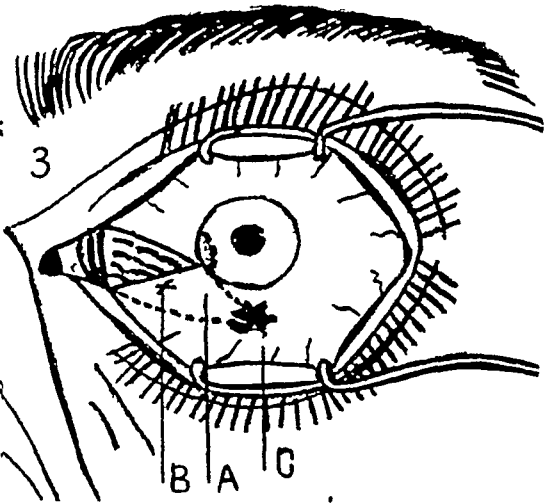
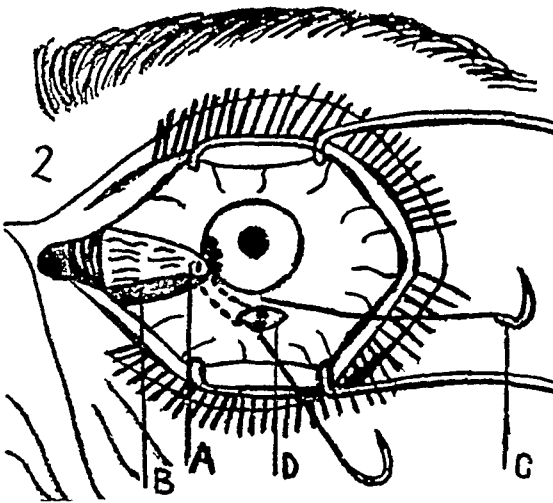
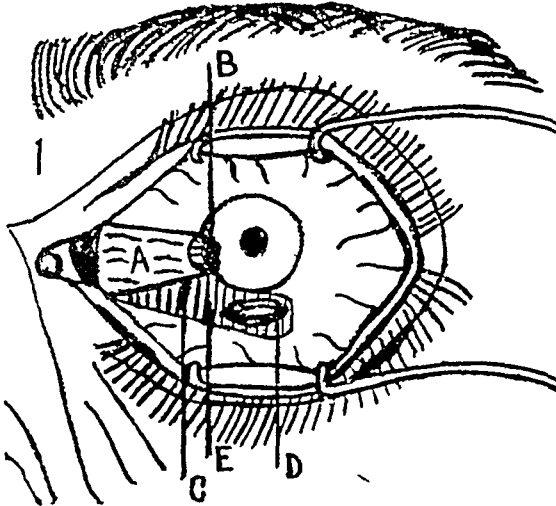
MODIFICATION OF THE McREYNOLDS TRANSPLANT OPERATION

The head of the pterygium is removed from the cornea as previously described, and the inferior margin of the neck and body of the pterygium is severed from the bulbar conjunctiva toward the canthus for a distance of from $\frac{1}{4}$ to $\frac{1}{2}$ inch (0.63 to 1.27 cm). The pterygium is then separated by blunt dissection from the subconjunctival tissue and a double-armed, atraumatic, 0000 chromic surgical gut suture is introduced from without inward through the head of the pterygium. Chromic surgical gut is employed for two reasons. 1. Since removal of chromic surgical gut sutures is unnecessary, manipulation is therefore avoided, and the production of a firm scar is thus assured. 2. The chemical irritation which is produced by the liberation of chromic acid about the suture is an additional factor in securing a relatively firm adhesion between the head and neck of the pterygium and the episcleral tissue.

The bulbar conjunctiva below is undermined toward 6 o'clock in a narrow strip, measuring 4 to 5 mm, thus causing a minimal disturbance

of the lymphatic drainage in this area (figure, 1) A number of surgeons undermine a large area, but this is unnecessary

An incision 5 mm in length, concentric with the limbal curvature, is made into the bulbar conjunctiva and Tenon's capsule and is placed 5 mm from the limbus The site for incision is previously gaged by grasping the head and placing it on the bulbar conjunctiva, after exert-



1, Narrow subconjunctival tunnel, *E*, leading to incision below, *D* *A* is the pterygium, *B*, the denuded corneal bed, and *C*, the inferior margin of the pterygium 2, chronic surgical gut suture, *C*, passed through the episclera, *D*, under direct observation, a mattress suture is placed in the pterygium, *A*, *B* is the episcleral site of the traction suture 3, the head of the buried pterygium, *A*, is firmly united to the episclera and the conjunctiva in one suture, *C*, *B* is a traction suture

ing a moderate pull on the pterygium The inferior and superior edges of this incision are undermined for 2 to 3 mm The previously prepared narrow subconjunctival tunnel, as described, is made to communicate with the conjunctival incision below The heels of the two needles

are brought through the tunnel to emerge in the incision. The bulbar conjunctiva is grasped with a fixation forceps and the eyeball held firmly for counterpressure. The inferior lip of the conjunctival incision is retracted downward, and the inferior needle is passed through episcleral tissue and Tenon's capsule under direct observation (figure, 2). A similar procedure is performed superiorly. A distance of 3 mm should separate the two episcleral bites, vertically. The suturing is completed after the two needles have passed through corresponding sites in the free edges of the incision. The head of the pterygium is then drawn through the tunnel and the suture tied firmly. Thus, only one suture is required to unite all the tissues (figure, 3). In employing the procedure as described, the chances of recurrence are reduced to a minimum. One need not employ the conjunctival suture, as described, for very small pterygia. After the body of the pterygium has been cut and a small subconjunctival tunnel made below, an assistant grasps and retracts the inferior conjunctival lip, so that an episcleral bite can be obtained under close observation.

It is advisable to employ a traction suture if excessive tension on the head of the pterygium is anticipated. This is accomplished in the following manner. The body is drawn upward after dissection of its inferior margin, bringing the underlying tissues into view. A small incision, measuring 4 mm, is made into Tenon's capsule, it lies perpendicular to, and 5 mm away from, the limbus. The line of incision parallels the inferior border of the pterygium. A double-armed, atraumatic, 0000 black silk suture is passed through the episcleral tissue so that the bites are separated for a distance of 4 mm. By placing the pterygium on stretch, one can determine the exact location for the passage of the underlying suture. The needles are then introduced into the free edge of the conjunctiva and the suture is tied. This suture fixes the middle of the body and produces relaxation of the tension on the head of the pterygium. If the pterygium is very large and broad, one may use two traction sutures to great advantage. The sutures are removed on the fifth to the seventh day. If one desires to retain these sutures for large pterygia, chromic surgical gut is substituted for black silk.

The redness of the conjunctiva persists from seven to ten days after the operation but is rarely associated with actual pain. In a small percentage of cases there is slight ocular discomfort, which has never been sufficiently pronounced to necessitate additional treatment. It is common to encounter a degree of bulbar injection in excess of that seen in the conventional McReynolds procedure. This is a source of no concern, since it is due simply to the desired chemical irritation of the chromic surgical gut.

SUMMARY

1 An explanation for recurrence of pterygiums is offered

2 A new modification of the McReynolds transplantation for pterygium is presented Use of this new procedure reduces the number of recurrences to a minimum

3 A traction suture for broad and large pterygiums is described

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ARACHNOIDITIS

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ARACHNOIDITIS is a comparatively new entity in the field of neuro-ophthalmology. It is an inflammation of the leptomeninges, which may be localized or diffuse, even to the extent of involving the entire central nervous system.

HISTORICAL REVIEW

The pathology of the serous form of meningitis was first described by Quincke in 1893, and in 1898 Schlesinger¹ described the localized cystic form. It was Horrax,² working at Cushing's clinic, who gave this condition a new clinical interpretation when he presented 33 cases of pseudocerebellar tumors which on operation proved to be cases of arachnoiditis.

In 1929 Cushing and Eisenhardt³ were the first to recognize the chiasmic form when, in one of the classic monographs on chiasmal tumors emanating from Cushing's clinic, they mentioned chronic cisternal arachnoiditis as a condition to be differentiated from tumors of the chiasm. However, the importance of this contribution was overlooked in the larger and more important aspects of the paper. In the same year Holmes⁴ presented 2 cases of arachnoiditis in which he successfully operated for failing vision, but it was Balado and Satanowsky⁵ who reported the first case of chiasmic arachnoiditis on record in which operation was successfully performed.

ETIOLOGY

Cushing⁶ early recognized that infections could play an important part in causing arachnoiditis in the chiasmal region, and he stated that

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1 Schlesinger, A. Beitrage zur Klinik der Rückenmarks und Wirbeltumoren, Jena, Gustav Fischer, 1898

2 Horrax, G. Generalized Cisternal Arachnoiditis Simulating Cerebellar Tumor, Arch Surg 9 95 (July) 1924

3 Cushing, H., and Eisenhardt, L. Meningiomas Arising from the Tuberculum Sellae, Arch Ophth 1:1 (Jan.), 168 (Feb.) 1929

4 Holmes, G. Suprasellar Tumors, Internat Cong Ophth (1929) 3:65, 1930

5 Balado, M., and Satanowsky, P. Tratamiento quirurgico de la atrofia de la papila, Arch argent de neurol 4 71 (March) 1929

6 Cushing, H. The Chiasmal Syndrome, Arch Ophth 3 305 (May), 704 (June) 1930

diseases of the paranasal sinuses, because of their location, were an important etiologic factor. Bollack, David and Puech⁷ were able to trace the probable cause in only 81 out of 129 cases of arachnoiditis reported by them. There was an antecedent history of trauma in 15 per cent, and in the remainder an infection or a toxic condition was the causative agent. Diseases of the sinuses, nose and tonsils led, with 13 per cent, syphilis was second, with 9 per cent, followed by otitis, with 5 per cent and tuberculosis, with 4 per cent, and the rest of the cases were scattered among many other morbid conditions, such as rheumatic fever, influenza, dental infections, pregnancy and alcoholism. A study of the literature shows a general agreement with these figures.

Trauma, especially to the head, seems to play a definite, though at times a doubtful, part, for, as Bollack, David and Puech pointed out, there does not seem to be any definite relation between the location, the intensity of the trauma or the time interval and the subsequent development of the arachnoiditis. Thus, Goldsmith⁸ reported 3 cases of traumatic origin. In 1 case there was a history of injury followed by unconsciousness eleven years before the onset of symptoms. In the second case the symptoms came on immediately after the patient regained consciousness from a head injury, and in the third the symptoms appeared four months after a fall which slightly dazed the patient. In other cases reported the condition had apparently followed injuries even more trivial than the latter, and in evaluating the history of trauma one must bear in mind that the vast majority of people at some time or other have had trauma to the head.

Hausman,⁹ more than any one else, brought out the importance of syphilis as a cause of arachnoiditis. In several papers, he pointed out the fact that syphilitic arachnoiditis is no different from arachnoiditis from any other cause. Bollack, David and Puech also found that the majority of the cerebromeningeal forms of arachnoiditis were syphilitic in origin.

As previously mentioned, infections of the nasal and paranasal sinuses are the most frequent cause of arachnoiditis, but unusual sources of infection should not be overlooked. In 1 of my cases the condition apparently followed severe chilling from exposure to the rain. Baillart, David and Schiff-Wertheimer¹⁰ reported the case of a man

7 Bollack, J, David, M, and Puech, P. *Les arachnoïdites opto-chiasmatiques*, Paris, Masson & Cie, 1937.

8 Goldsmith, A J B. Chiasmal Arachnoiditis, *Proc Roy Soc Med* **36** 163 (Feb) 1943.

9 Hausman, L. Syphilitic Arachnoiditis of the Optic Chiasm, *Arch Neurol & Psychiat* **37** 929 (April) 1937.

10 Baillart, P, David, and Schiff-Wertheimer. Arachnoïdite opto-chiasmatique avec cécité totale, *Bull Soc d'opht de Paris*, June 1934, p 293.

who had rapid loss of vision and palsy of the third nerve on the left side following removal of a left lower molar tooth. Operation revealed arachnoiditis localized to the chiasmic region.

PATHOLOGY AND MORBID ANATOMY

Normally, there is a space between the pia and the arachnoid, the subarachnoid space, and between the two layers there are numerous fine fibrous strands, called the arachnoidal trabeculae. Sometimes the subarachnoid space is so narrow that the two layers appear as one, an inner vascular portion (pia) and an outer, thicker vascular layer (arachnoid).

Arachnoiditis, or inflammation of these membranes, is either adhesive or cystic in form. The cysts are collections of cerebrospinal fluid walled off by adhesions, and the fluid may at times be under great tension. The adhesive form is characterized by dense adhesions, which may bind the optic nerves and chiasm to any or all of the surrounding structures and in the advanced stage calcareous plaques and small cysts are usually present. The inflammation may involve either the pia or the arachnoid alone, but in the vast majority the two layers are simultaneously affected. Usually, the subarachnoid space is entirely obliterated, but in the areas where the inflammation is less severe some traces of the space may be found, while in cases of very severe inflammation even the subdural space is obliterated and the arachnoid becomes acellular and is composed of dense collagenous tissue.

The optic nerves and chiasm are usually involved in the opticochiasmic type of the disease. The appearance of the nerves is somewhat unusual in that in most cases there seems to be a combination of primary and secondary atrophy. This peculiar combination is a result of increased intracranial pressure, and at the same time adhesions are constricting the chiasm or the nerves or both. In addition, as Spaeth¹¹ has shown, there may be marked distortion of the blood vessels in that region, with interference of the blood supply to the delicate nerve structures.

SYMPTOMS

The symptoms to a considerable extent depend on the location, extent and severity of the lesions. Headache is frequent with arachnoiditis, it may be present in any part of the head and is usually severe. To the ophthalmologist the visual symptoms are of paramount importance. In the opticochiasmatic form of arachnoiditis sight is frequently jeopardized and the disks are rarely normal. There may be primary, secondary or a segmental type of atrophy of the optic nerve,

¹¹ Spaeth, E. R. Swelling of the Nerve Heads with Arachnoiditis and Unusual Changes in the Visual Fields, *Arch Ophth* 12:167 (Aug) 1934

or even extreme degrees of choked disk, or any combination or gradation of these signs

A central scotoma is common, being present in 31 per cent of the cases reported by Bollack, David and Puech, a finding corroborated by most authors. Cushing stated that the presence of a large central scotoma in cases of suspected chiasmal lesions is in favor of a diagnosis other than tumor.

Occasionally one sees typical bitemporal field defects, but more often they are bizarre because of extensive involvement of the nerves, chiasm and surrounding blood vessels by adhesions. In Spaeth's case there were binasal field defects, and on operation the large blood vessels were observed to be bound down to the sella turcica. Similar field defects have been reported by others. Unusual altitudinal field defects have been observed by a number of authors.

However, the most outstanding symptom in this form of arachnoiditis is the early, and usually rapid, loss of vision, sometimes involving one eye before the other. This loss is often so rapid and so extensive that one must agree with Hartmann¹² that in some cases the loss of vision is due not only to pressure on the optic nerves and chiasm but to actual involvement of these structures in the inflammatory process. In some cases impairment of the blood supply may be an important factor in the loss of vision.

With the visual changes, there may be all the symptoms characteristic of chromophobic adenoma of the anterior lobe of the pituitary gland or of a suprasellar cyst: polydipsia, polyuria, hyperthermia, obesity of the Frohlich type (sex infantilism) and dyspituitarism. Barcala¹³ reported the case of a youth aged 15 who presented a typical Frohlich syndrome, but with edema of the disks, central scotomas and normal peripheral fields.

If the arachnoiditis is more anterior, symptoms referable to tumor of the frontal lobe may be simulated, i.e., anosmia and a more or less typical Foster Kennedy syndrome. Baillart and Schiff-Wertheimer's case presented a typical Foster Kennedy syndrome, and Vail¹⁴ was able to collect several similar cases from the literature.

The symptoms in other forms of arachnoiditis vary greatly. Ocular motor paralyses are frequent. Occasionally choked disks may be the only ocular finding, or the fundi may be entirely normal. At times arachnoiditis may simulate cerebral tumor so closely that the true path-

12 Hartmann, E. Optochiasmic Arachnoiditis, *Arch Ophth* **33** 68 (Jan) 1945

13 Barcala, F. J. Síndrome de Froehlich pseudotumoral con arachnoiditis quiasmática, *Semana med* **2** 498 (Aug 26) 1943

14 Vail, D. Optochiasmic Arachnoiditis, *Arch Ophth* **20** 384 (Sept) 1938
Heurer, G. J., and Vail, D. T., Jr. Chronic Cisternal Arachnoiditis Producing Symptoms of Involvement of Optic Nerves and Chiasm, *ibid* **5** 334 (March) 1931

ologic process is not revealed until operation is performed. This is particularly true, as Demel¹⁵ has shown, of the localized types of arachnoiditis, with which there may be choked disks, vomiting and epileptiform attacks, or the convulsions may be jacksonian in type.

PROGNOSIS

The prognosis on the whole is good, especially as regards vision, if operation is resorted to early. Of course, if the condition has lasted too long, the loss of vision becomes irrevocable. As previously pointed out, in some cases the loss of vision is due to actual inflammation of the nerves and chiasm. In such cases the prognosis is poor, and, as the presence of such a process cannot be predicted, the preoperative prognosis should be guarded.

DIAGNOSIS

Because of its polymorphous manifestations, the diagnosis of arachnoiditis is not easy. The chiasmic type gives symptoms referable to pressure in that region. However, unlike the changes of true tumors of the pituitary gland, the sella turcica is usually normal on roentgenographic examination, and typical bitemporal field defects are rare. The rapidity of development of the visual symptoms favors the diagnosis of arachnoiditis rather than tumor. In addition, the disks, instead of primary atrophy, show a peculiar mixture of primary and secondary atrophy, often with moderate edema. This feature was strongly stressed by di Marzio, Cavina and di Nigris,¹⁶ Bollack, David and Puech,⁷ Vail,¹⁴ Lillie,¹⁷ Haitmann¹² and others.

From the demyelinating diseases, such as multiple sclerosis, arachnoiditis is differentiated by absence of a history of remissions and by the neurologic signs and from Devic's and Schilder's disease (optic neuroencephalomyelopathy and progressive subcortical encephalopathy) by their typical course after the initial onset. In Leber's optic atrophy there is a hereditary factor, and blindness is never complete. In the toxic amblyopias there is early loss of central vision and the fundi usually remain normal for a long time. Optic neuritis from sinus infection is more difficult to exclude, for this condition is a cause of arachnoiditis. If infection is present, the sinuses should be cleaned out before further exploration is undertaken. Encephalographic and ven-

15 Demel, R. Die Meningitis serosa circumscripta cerebialis unter dem Bilde des Hirntumors und ein Beitrag zur ihrer Aetiologie, *Arch f klin Chir* **125** 561 (Sept.) 1923.

16 di Marzio, Q., Cavina, C., and di Nigris, G. Sulla aracnoidite opto-chiasmatica, *Riv oto-neuro-oftal* **13** 291 (July-Aug.) 1936.

17 Lillie, W. I. Prechiasmal Syndrome Produced by Chronic Local Arachnoiditis, *Arch Ophth* **24** 940 (Nov.) 1940.

triculographic studies are important because they may show abnormality of the cisternal and ventricular systems

TREATMENT

Rubino¹⁸ claimed that in 3 cases vision improved with intravenous injections of iodides. However, he and all other authors unanimously agreed that the treatment for this condition is primarily surgical. This becomes imperative if great loss of vision is threatened, and it is important to remember, as Hausman has shown, that the same treatment is essential in the arachnoiditis due to syphilis. David, Hartmann and Hébert¹⁹ also stressed this point, and they further stated that even in tabes the loss of vision may be due to arachnoiditis. They reported a case of tabes in which loss of vision in the lower fields developed. At operation arachnoiditis was found, and when the adhesions around the nerves were separated there was some recovery of vision. However, it is difficult to decide when to operate in these cases. On the whole, as the aforementioned authors pointed out, if conservative treatment fails, operative treatment is advisable because of the threat to vision. Surgical separation of the arachnoidal adhesions has effected a cure in cases of epilepsy and convulsions which were due to focal irritations of the cortex. One must also remember that long-standing choked disks result in secondary atrophy and blindness and that, in the absence of localizing signs, trephination to relieve intracranial pressure may ward off threatened blindness.

REPORT OF CASES

CASE 1—M G, a man aged 24, was admitted to the New York Post-Graduate Hospital on Aug 18, 1939, with a history of major and minor convulsive attacks since early childhood. He also complained of blurred vision and was partially deaf. The convulsive attacks had their onset in early childhood following a fever for a short period, during which he had two convulsions.

Neurologic examination revealed nothing significant except that the convulsions seemed to be initiated in the left cortex. The vision, visual fields and fundi were normal.

The encephalogram, taken on August 21, was reported to show that the bones of the vault were rather thick and dense with moderate hyperostosis on the inner table in both frontal regions. The sella turcica was smaller than normal. The ventricular system was enlarged but symmetric, and there was definite evidence of cortical retraction.

The patient was discharged because no definite diagnosis was made, but, as he continued to have numerous minor and a few major convulsive seizures,

18 Rubino, A. Contributo allo studio dell'aracnoidite ottico-chiasmatica, *Riv oto-neuro-oftal* 14 552 (Nov-Dec) 1937.

19 David, M., Hartmann, E., and Hébert, E. Arachnoidite et compression vasculaire du chiasma chez un tabétique, *Bull Soc d'opht de Paris*, December 1936, p 789.

he was readmitted on Nov 23, 1939, for further study. Again, the neurologic and ophthalmic examinations showed nothing abnormal, and a second encephalogram showed no change from the preceding one. The patient was discharged without a diagnosis.

He was readmitted on March 27, 1940 because the convulsions had increased in frequency. It was decided to open the cranium over the left frontal area and search for a localized focus of irritation. This was done by Dr J A MacLean on March 28. Extensive arachnoidal adhesions were observed and were freed with great difficulty.

When he was last seen at the clinic, on March 5, 1942, he stated that he had had no attacks since the operation.

This is an interesting case of chronic adhesive arachnoiditis in which, in spite of extensive involvement of the anterior part of the brain, no part of the visual pathways was involved and no neurologic signs were present except for a focal irritation of the brain.

CASE 2—M W, a woman aged 29, came to the Post-Graduate Hospital on March 3, 1929, because of menstrual disturbances for the past six years and failing vision for the past four years.

Previous to the onset of symptoms her menses came regularly every twenty-eight days and lasted four days. Now they came every two weeks and lasted one day. The visual disturbances began with blurring in one eye and then in the other, and vision had deteriorated steadily since the onset.

Neurologic examination revealed nothing abnormal, but ophthalmic examination showed pallor of both disks and left homonymous hemianopsia. Operation was performed for tumor of the pituitary gland but none was found, and the patient was discharged after recovery from the operation.

Unfortunately, all the original records were lost, so that more detailed information is not available.

She was readmitted on Oct 14, 1930, with the history that after operation vision had failed more rapidly and she had gained considerably in weight, about 63 pounds (28.6 Kg). She had not had her menses since the operation. For the past five months she had had polyuria and polydipsia.

An encephalogram revealed a normal ventricular system and normal sella turcica, and she was again discharged for further care in the outpatient department. She was placed under mixed glandular therapy, and at intervals roentgenograms of the skull were taken. These always revealed no pathologic change.

The patient was readmitted to the hospital on Aug 11, 1933 because her symptoms had become worse. Examination of the eyes showed a mixed type of primary and secondary atrophy of the optic nerve. The right eye was blind, and only an island of vision was retained in the temporal field of the left eye. A ventriculogram, taken on August 21, revealed dilatation of the left ventricle with cortical atrophy. The right ventricle was normal.

Operation on August 31, by Dr John Scarf, revealed extensive chiasmic arachnoiditis, with a large cyst which had lifted the chiasm upward. The cyst was emptied and the adhesions were ruptured, but the patient's condition was not improved. When she was last seen, on April 2, 1942, there were progressively increasing drowsiness and great impairment of memory.

The first operation was performed before the entity of chronic arachnoiditis was well known. If the adhesions had been separated then,

the subsequent course of the patient's condition might well have been different

CASE 3—F D, a girl aged 17 years, came to the Brooklyn Hospital on May 4, 1937, because of transitory attacks of blurred vision and progressive loss of sight for the past four months

About ten months before admission, the patient awoke one night and vomited three or four times. She was very dizzy and had pain over the left eye. The next morning she was well. Five months later, she had tinnitus in the right ear, which lasted over an hour. She described her attacks of blurred vision as a feeling that she was looking through a fog. The visual disturbances had been occurring with increasing frequency. Three weeks before admittance she had an attack of blurred vision which was accompanied with such dizziness that she fell. Her menstrual periods started at the age of fourteen years and had occurred regularly every twenty-eight days until three months before her admission, when they became scanty and occurred every two weeks.

Examination—The patient had a large amount of pubic hair and a moderate streak of hair extending up to the umbilicus. Her arms, legs and thighs were also hairy. There was slight diminution of sensation over the right side of the face and a suggestion of weakness of the right side of the face during the emotional phase.

Ophthalmic Examination—Vision was 13/200 in the right eye and was limited to counting fingers at 6 inches (15 cm). There were no ocular palsies and no nystagmus. The right pupil reacted well to light and the left sluggishly, both reacted in accommodation. The right disk was swollen about 3 D, and there was pronounced secondary atrophy of the disk. The left disk was less edematous but showed a greater amount of atrophy. The right field was markedly and irregularly contracted for a 20 mm test object. There was an island remaining in the left field with a 40 mm test object.

Flat roentgenograms, taken on May 5, showed that the bones of the skull had a wavy unevenness in density. The suture lines, especially the occipital, were separated. A ventriculogram taken on May 12 showed that the lateral and third ventricles were greatly distended but normal in position. The cerebral aqueduct and the fourth ventricle were not visualized.

The impression was that of obstruction below the third ventricle.

A preoperative diagnosis of chronic arachnoiditis was made, and a posterior craniotomy was done by Dr E J Browder the same day. Extensive adhesive arachnoiditis was observed. The adhesions could not be separated, so the area was left decompressed.

After recovery, the patient was discharged to the outpatient department, where she was under observation about three years. From time to time the decompressed area bulged considerably because of episodes of increased intracranial pressure, but her headaches and vomiting disappeared and with time her vision and visual fields improved. At the last examination, on Feb 28, 1940, vision was 20/100 in the right eye and 5/200 in the left eye, and the right visual field had improved considerably, although the optic disk appeared to be more atrophic. Since operation she had had no headaches, dizziness or vomiting.

CASE 4—A M, a woman aged 24, came to the Post-Graduate Hospital on Aug 16, 1937, because of headaches, blurring of vision and nausea of four months' duration.

The symptoms started shortly after a third operation on the right mastoid with an attack of blurred vision, which lasted about fifteen minutes and was followed by a period of freedom from symptoms for about two weeks. Then the attacks of blurred vision became more frequent and severer. Most of the attacks were followed by right-sided headaches, which lasted three or four days and were accompanied with nausea and vomiting. The patient also stated that at times she saw double.

Except for impaired smell in the right nostril and impaired hearing on the right side, the neurologic examination revealed nothing abnormal. The patient had normal vision and visual fields, and the fundi appeared normal.

An encephalogram, taken on August 18, showed a normal state except that the sella turcica was 20 per cent undersized.

The patient was discharged without a diagnosis and was readmitted on September 24 because, in addition to the aforementioned symptoms, severe tinnitus had developed on the right side. A block of the right stellate ganglion was done by Dr J. A. MacLean, with relief of symptoms for several months.

On June 7, 1938, the optic disks began to appear engorged, and spinal tap verified the presence of increased intracranial pressure. A craniotomy in the region of the right mastoid revealed a large arachnoid cyst. This was evacuated and the adhesions were ruptured. The patient has remained well since.

CASE 5—H. T., a man aged 28, was admitted to the Post-Graduate Hospital on Oct. 11, 1939, with a history of convulsions for the past two years. The convulsions started with a cramp in the left leg and spread upward to the arm. The face was never involved. The convulsions were followed by loss of consciousness, which lasted three or four minutes. There was no biting of the tongue or frothing at the mouth. He gave no history of trauma.

A neurologist had sent the patient to the hospital with a diagnosis of jacksonian epilepsy and had made a preoperative diagnosis of parasagittal meningioma.

An encephalogram, taken on October 13, showed slight flattening of the lateral ventricles. Ophthalmic examinations revealed only a slight contraction of the fields.

A craniotomy over the right parietal area, by Dr J. A. MacLean, revealed localized chronic adhesive arachnoiditis, which was secondary to an old sub-arachnoid hemorrhage (traumatic). The scar tissue was excised from the involved area. Since the operation the patient has had only occasional convulsive attacks.

CASE 6—S. L., a man aged 40, was admitted to the Post-Graduate Hospital on Dec. 15, 1934, with a history of diplopia for the past two years and headaches for the past two weeks. With these headaches there were frequent attacks of nonprojectile vomiting. In addition, for the past ten months he had yawned frequently, and for the past few months he had had frequent attacks of hiccup. For a long time there were mild occipital and frontal headaches, but for the past two weeks these headaches had become extremely severe, especially on moving the head. About two years before, shortly before the symptoms started, he was injured while riding in a taxicab. He was not unconscious but had severe headaches for a few days.

Examination—The patient was drowsy but responded to questions. The right upper lid was ptosed, and the left lateral rectus muscle was paretic. There was a marked lateral nystagmus to the left, with the rapid component to the medial side. The nystagmus to the right was slight. The pupils were equal and regular and reacted to light and in accommodation. The right disk was slightly blurred,

and the left was normal. The visual fields and visual acuity could not be determined. Neurologic examination revealed nothing abnormal except for a slight increase in the reflexes on the right side. Flat roentgenograms of the head showed a normal condition.

On Jan 14, 1935, the disks, especially the right, showed increased edema. In a ventriculogram, taken on January 23, the third ventricle was not visualized, and a diagnosis of tumor of the third ventricle was made. A suboccipital craniotomy, done on the same day by Dr J A MacLean, revealed extensive chronic adhesive arachnoiditis. The patient did not respond after operation and died a few days later. Permission for autopsy was not obtained.

CASE 7—M D₁ B, a girl aged 7 years, was admitted to the Post-Graduate Hospital on Oct 13, 1936, because of frequent vomiting and occasional headaches for the past three weeks.

About a week prior to the onset of symptoms the child had come from school in a cold drizzling rain and had received a thorough wetting. That night she had chills and for the next two weeks had a cold, without fever. A week before hospitalization she fell and struck her head, but not severely.

Examination—The right pupil was larger than the left, and the corneal reflex was absent on the left side. The left lateral rectus muscle was completely paretic. The right disk was slightly blurred, and the left disk was normal. Neurologic examination revealed rigidity of the neck and deviation of the tongue to the left. There was weakness of the right side of the face, a Babinski sign on the right side and a questionable Babinski sign on the left.

On October 16, the right disk was swollen about 5 D and the left disk about 1 D. A ventriculogram, made that day, showed blocking in the cerebellar area.

A suboccipital craniotomy, performed by Dr John Scarf the next day, revealed extensive cystic arachnoiditis in the region of the fourth ventricle. The cyst exerted great pressure on the cerebellum, and the foramina of Magendie and Luschka were closed by adhesions. The cyst was evacuated and the adhesions were separated. The child did not respond after the operation and died two days later. Permission for autopsy was not obtained.

CASE 8—M G, a woman aged 22, came to the Post-Graduate Hospital on March 2, 1937, with a history of nausea, vomiting and headaches for the past two years. The symptoms followed shortly after operation for acute appendicitis. The headaches were severe and were localized to the left side of the head. The vomiting was not projectile.

Ophthalmic and neurologic examinations revealed a normal state, and a ventriculogram, made on March 4, showed no evidence of a lesion encroaching on the ventricular system. Dr J A MacLean, therefore, injected the stellate ganglion, thus giving symptomatic relief to the patient, and she was discharged from the hospital. The patient returned to the outpatient department, where the ganglion was blocked several times, always giving her symptomatic relief.

On September 24, with the patient under anesthesia induced with solution of tribromoethanol U S P and oxygen, a preganglionic section of the superior cervical sympathetic ganglion was done and the presence of chronic adhesive arachnoiditis was noted. No further surgical measure has been attempted because the patient has been free of headaches to date.

CASE 9—A J M, a man aged 44, came to my office on Nov 19, 1935 with a history of headaches for over twenty years. About five years before his admission the headaches became very severe and he vomited several times. He was

told that he had sinusitis and he underwent treatment. For the few months preceding admission, he had had severe dizzy spells several times daily, and he fell on two occasions. Lately, print seemed to "fly" and appeared blurred.

Examination—Vision was 5/200, improved to 20/25, in the right eye, and 5/200, improved to 20/50, in the left eye. The right disk showed choking of about 5 D, with a few hemorrhages around it, and the left was swollen about 2 D. The blindspots were enlarged, but the peripheral fields were full and showed no localizing defects.

A tentative diagnosis of tumor of the frontal lobe was made, and the patient was referred for neurologic examination. This showed nothing significant.

The patient's vision deteriorated rapidly. A thorough examination, including ventriculograms, at the Johns Hopkins Hospital, revealed no localizing lesion. On November 26 Dr. Walter Dandy made a trephine opening over the right parietal area and probed for a tumor but found none. A diagnosis of arachnoiditis was made, and the trephine opening in the bone was left open. Dr. Dandy felt that if the intracranial pressure had not been relieved secondary atrophy of the nerve and blindness would have resulted.

The patient has been under constant observation since and was last examined on June 11, 1945. Vision has remained at 20/20 with correction in both eyes, the peripheral fields are full, but the blindspots are still enlarged. At times the area of trephination is soft, at other times it is rather hard, so that the brain herniates through the wound and feels tense. At such times one can feel, and even see, pulsations of the herniated part of the brain, and the patient usually has headache and feels nauseated. These symptoms are accentuated by even the slightest pressure over the herniated area. The disks during these episodes become engorged, but this feature is not constant. The borders of the disks are not well outlined, but there is no evidence of secondary atrophy. According to the patient, the intracranial pressure seems to be affected greatly by changes in the weather.

CONCLUSION

Arachnoiditis is not so rare an entity as is commonly thought. At the New York Post-Graduate Medical School and Hospital between 1935 and 1940, inclusive, there were 118 cases of suspected neoplasm, in 67 of these cases the condition was definitely diagnosed as neoplasm, and in 11, arachnoiditis, that is in 14 per cent of the total number of cases in which a diagnosis was made.

Judging from the number of papers in the literature, there has been an increasing awareness of this condition among ophthalmologists. However, the criteria for its diagnosis are still difficult, and in too many cases the necessary surgical treatment is not carried out. The greatest difficulty lies in the differentiation of cases of arachnoiditis from the unfortunately large number of cases in which the optic nerves are directly involved and the process is not arachnoiditis. It is small comfort to a patient to undergo a formidable operation on the head because of a mistaken diagnosis. Fortunately, neurosurgery has advanced to such a degree that the operative and postoperative mortality rates are very small. Every ophthalmologist has permitted loss of vision to progress to complete blindness as he stood helplessly by, because

the roentgenograms of the sinuses did not reveal any disease process and no localizing signs were present. Early surgical intervention in some of the cases might have saved vision.

It must also be emphasized that, though opticochiasmic arachnoiditis presents a great threat to vision, other forms of arachnoiditis can be as great a threat, as cases 3 and 9 show. One can speculate as to what would have happened if the patient in case 3 had come for treatment at an earlier time.

Because ophthalmologists are usually consulted by the neurosurgeon in all cases of suspected tumor of the brain, they must be aware of the fact that localized arachnoiditis can simulate a tumor of any part of the brain. These lesions are less likely to cause field defects because the cortex is irritated by scars from the membranes covering the brain and are therefore superficial.

With the increasing attention given this subject, it is hoped that with time arachnoiditis will be more easily diagnosed. Vision is so important a function that if a case presents the possibility of arachnoiditis surgical measures should not be postponed until too late.

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EXOPHTHALMOS AND ASSOCIATED OCULAR DISTURBANCES IN HYPERTHYROIDISM

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WHEN Marine and his associates¹ produced chronic progressive bilateral exophthalmos by daily intramuscular injections of 0.05 to 0.1 cc of methyl cyanide in 2 to 3 month old rabbits maintained on a diet of alfalfa, hay and oats, he came to the following conclusion

Cyanides appear to act by inhibiting metabolic processes. This inhibition stimulates the hypothalamic centers which in turn, stimulate the pituitary to produce the thyrotropic hormone, which in turn stimulates the thyroid gland and independently the sympathetic centers in the mid-brain, causing exophthalmos.

It occurred to us that since pupillography, as devised by Lowenstein and associates,² can show evidences of central sympathetic disturbances, it might be advantageous to determine what these changes are which occur with hyperthyroidism. Accordingly, 22 patients were studied, these included patients with and without exophthalmos and patients with unilateral exophthalmos. The results were interesting (fig 1). All but 1 patient showed a miosis block, interpreted by Lowenstein as evidence of central sympathetic disturbance. No explanation can be given at present as to why this patient did not show this pattern. However, the appearance in practically all cases suggested further value for this test. Occasionally in cases of unilateral exophthalmos the general evidences of hyperthyroidism may not be apparent or may be borderline. It seemed that a positive pupillographic

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1 Marine, D., and Rosen, S. H. Exophthalmos in Thyroidectomized Guinea Pigs by Thyrotropic Substance of Anterior Pituitary, and Mechanism Involved, *Proc Soc Exper Biol & Med* **30** 901 (April) 1933

2 Lowenstein, O., and Friedman, E. D. Pupillographic Studies, *Arch Ophth* **27** 969 (May) 1942, Adie's Syndrome (Pupillotonic Pseudotabes), *ibid* **28** 1042 (Dec) 1942. Lowenstein, O., and Givner, I. Pupillary Reflex to Darkness, *ibid* **30** 603 (Nov) 1943. Lowenstein, O., and Levine, A. S. Pupillographic Studies, *ibid* **31** 74 (Jan) 1944, The Role of the Sympathetic in the Light of Pharmacopupillographic Studies, *Proc Rudolf Virchow M Soc*, 1943, vol 2, p 82

curve might add to the information at hand. Accordingly, pupillographic studies were made on 5 patients without hyperthyroidism who had unilateral exophthalmos due to various causes, such as meningioma of

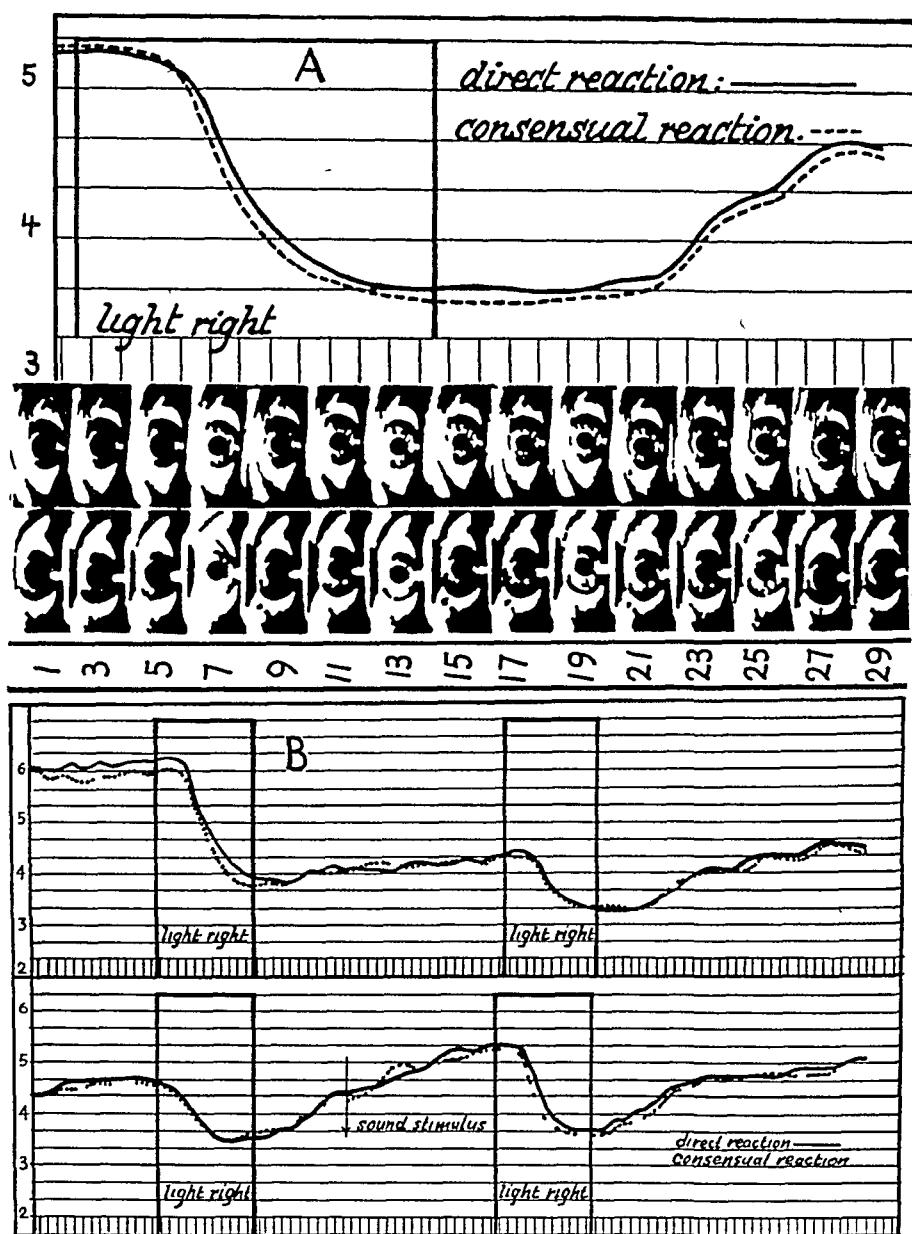


Fig 1—*A*, normal pupillographic curve, showing a period of latency, a contraction, a period of latency and a redilation. *B*, pupillographic curve in a case of hyperthyroidism, showing a period of latency, and a contraction, a period of latency and a redilation block.

the sphenoidal ridge and hemangioma of the orbit. The unilateral exophthalmos of 1 patient was unexplained. For all patients studied normal curves were found. The additional case of a nurse (R. W.)

in whom unilateral exophthalmos had developed is worthy of note. A pupillographic study showed a typical redilation block, suggesting that this case probably was one of hyperthyroidism.

REPORT OF CASES

CASE 1—R W, a nurse, single, aged 31, first noticed exophthalmos of the right eye in July 1943. The basal metabolic rate was 4 per cent above the average normal. A roentgenogram of the sphenoidal ridge, the orbit and the thymus revealed nothing abnormal. On Dec 9, 1943, the right palpebral aperture was 11 mm and the left 9 mm. With the Hertel exophthalmometer at 100 mm, exophthalmos measured 20 mm in the right eye and 19 mm in the left eye. There were a fine tremor of the fingers and sweating of the hands. Pupillographic study showed an incomplete dilation block on both sides. Anisocoria of sympathetic origin existed. The conclusion was that since the pupillographic study revealed a bilateral condition the lesion was probably present in the hypothalamic region. On Jan 4, 1945, with the base line at 100 mm, the right eye measured 19 mm and the left eye 18 mm. The value of pupillography in the diagnosis of unilateral exophthalmos can only be established after many more similar cases are studied and followed through their course of development.

The evidence accumulated by Mulvaney³ supports his contention that the immediate cause of exophthalmos, whether it be of the thyrotoxic or of the thyrotropic type, resides in the extraocular and smooth muscles of the eyeball, Tenon's capsule and the lid. In the case of thyrotoxic exophthalmos, it is essential to know whether, in addition to removal of the sympatheticonia and lowering of the thyroxin content of the blood, the flabbiness of the muscles, with loss of striation, granular changes in the sarcoplasm and alterations in the neurolemmal sheaths, can be reversed. In the case of thyrotropic exophthalmos, can the round cell infiltration and fibrosis be lessened? Since neostigmine has been of value in treatment of myasthenia gravis and atony of the bladder and intestinal wall, 5 patients with hyperthyroidism were given 15 mg of neostigmine bromide orally three times daily for three to four months. The drug was administered postoperatively, when all factors but the essential changes in the muscles themselves had apparently been brought nearer to normal. No measurable reduction of the exophthalmos was noted. Since vitamin E had been suggested in the treatment of the muscular dystrophies, this vitamin, in the form of the acetate ester of alpha tocopherol (Ephynal acetate), was administered orally in doses of 25 mg three times daily for six weeks to 5 patients with hyperthyroidism. Here, again, the medication proved of no value. Similar negative results were obtained following the oral administration of 25 mg of pyridoxine hydrochloride three times daily for six weeks to 5 patients with hyperthyroidism.

3 Mulvaney, J H. Exophthalmos of Hyperthyroidism, *Am J Ophth* 27:589 (June) 1944.

On the introduction of thiouracil, it was hoped that with the reduction of the basal metabolism in patients seen early enough the exophthalmos would also recede. Results to date have proved otherwise. Even in cases in which most features of hyperthyroidism were abolished the exophthalmos either remained the same or increased. With thiouracil, changes in the pituitary gland have been noted which simulate those following thyroidectomy. Under the influence of this drug, the iodine content of the thyroid gland is rapidly depleted. The drug interferes with the synthesis of thyroxin in the thyroid gland, the glandular hyperplasia is a response to the lack of thyroid hormone, and this cannot take place in the absence of the hypophysis or, presumably, without the intermediation of the thyrotropic hormone of the anterior lobe of the pituitary.

To offset the pessimistic view that exophthalmos once established will not recede, it should be noted that exophthalmos has been reversed in some cases following the administration of iodine and during pregnancy. As proved by measurements with the exophthalmometer, the administration of iodine orally for several months reduced the exophthalmos in 3 patients.

The case in which exophthalmos was influenced by pregnancy is now reported.

CASE 2—I F, a white woman aged 34, noted an increase in her exophthalmos following thyroidectomy for hyperthyroidism, the degree of which finally became stabilized. She subsequently became pregnant. At the beginning of the second trimester the exophthalmos began to show improvement and continued to do so up to the time of delivery. Exophthalmometer readings showed that the exophthalmos had receded 4 mm, demonstrating that the changes in the extraocular muscles were reversible. Interestingly, the baby was born with exophthalmos, which did not recede fully until the age of 1 year.

Dr S S Ellenson⁴ gave the following report of a case.

L F, born of a mother with active hyperthyroidism, had a weight at birth of 5 pounds 3 ounces (2,353 Gm) and was premature in appearance. The infant had severe bilateral exophthalmos (fig 2). The pulse rate was over 200 a minute. She was hyperactive. She had repeated attacks of respiratory difficulty, reaching deep cyanosis with attacks of apnea. The infant was discharged on the tenth day with the mother but was readmitted four days later because of continued spells of cyanosis. She was placed in an incubator, with intermittent administration of oxygen. Her weight was 4 pounds 12 ounces (2,154 Gm). Twelve days later, having done well, weight 4 pounds 14 ounces (2,211 Gm), she was again sent home. The urine was normal. On April 4, 1942, a blood count showed 126 per cent hemoglobin, 6,750,000 red cells, 13,800 white cells, 62 per cent polymorphonuclear leukocytes, 30 lymphocytes and 8 per cent mononuclear cells. On April 11, the hemoglobin concentration was still 126 per cent, the red cell count was 6,300,000 and the white cell count 10,000, with 19 per cent

⁴ Private communication to the authors.

polymorphonuclear leukocytes, 72 per cent lymphocytes and 9 per cent mononuclear cells. She made slow, steady progress at home, weighing 18 pounds 12 ounces (8,504 Gm) at the age of 1 year. Some evidence of exophthalmos was still present. Centers of ossification in the wrist (two well formed bones) were normal for a child of her age. At 19 months of age she weighed 21 pounds 13 ounces (9,894 Gm). At the age of 2 years 9 months (Jan 14, 1944) her height was 36 inches (91 cm) and her weight 29 pounds (13.2 Kg). Fluoroscopic examination showed rapid bone development (four well formed bones in the wrist). There was no evidence of exophthalmos. The pulse was normal. The infant was normal in appearance and on physical examination. She has had the usual colds and sore throat (tonsillitis twice) and had responded normally to medication, including administration of ephedrine and sulfonamide drugs. The child is now 3 years old, and the mother's exophthalmos has stayed at a low level.

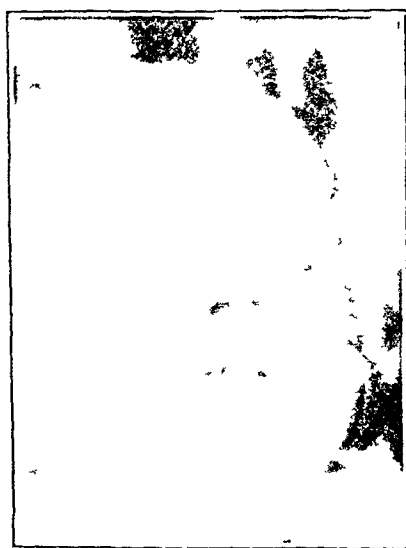


Fig 2—Baby L F at the age of a few weeks, showing 'the bilateral exophthalmos

This raises the question as to what happened during pregnancy which favorably influenced the exophthalmos. Did the baby's thyroid or thymus act for the mother? Were there certain hormonal changes occurring either at the placental barrier or in the mother which produced changes in the muscles of the eyes? We are not in a position to answer these questions, but they suggest material for investigation.

The use of ergotamine tartrate in selected cases to narrow the palpebral aperture should be mentioned.

CASE 3—S T, a woman aged 29, six years ago began to take thyroid to stimulate loss of weight. She became nervous, lost weight and acquired a stare. A diagnosis of hyperthyroidism was made, and thyroidectomy was performed. Soon after the operation the exophthalmos began to progress slowly. Nine months after operation her father became acutely ill, and the patient attended him constantly. She then noted a rapid progression of the exophthalmos, the amount reaching 30 mm in the right eye and 31 mm in the left eye, with the exophthalmometer at 110 mm. She was given 1 mm of ergotamine tartrate orally twice

a day, a temporary narrowing of the palpebral aperture was observed only while the drug was administered (fig 3)

Tearing, which is occasionally a distressing symptom in thyroid dyscrasias, was treated by the administration of tincture of belladonna 15 minims (0.93 cc) three times a day. The drug was valueless for relief of this symptom, and since it is possible that the dose is just sufficient to induce greater sympatheticonia (by abolishing the stabilizing vagotonia) the drug would seem to be contraindicated.

Chemosis, when observed, is due to venous obstruction. In an attempt to determine whether increased capillary permeability could be

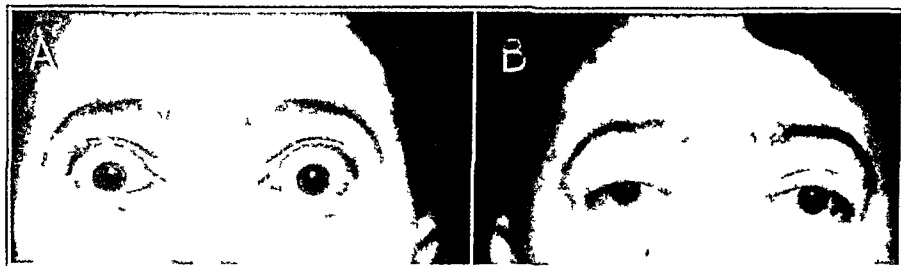


Fig 3 (case 3)—*A*, appearance of the palpebral aperture before the administration of 1 mg of ergotamine tartrate, *B*, appearance forty minutes later

demonstrated, Thiel's test was done (10 grains of fluorescein sodium every thirty minutes for three doses given by mouth). Observations with the slit lamp were made, but fluorescein failed to appear in either the anterior chamber or the chemotic conjunctiva.

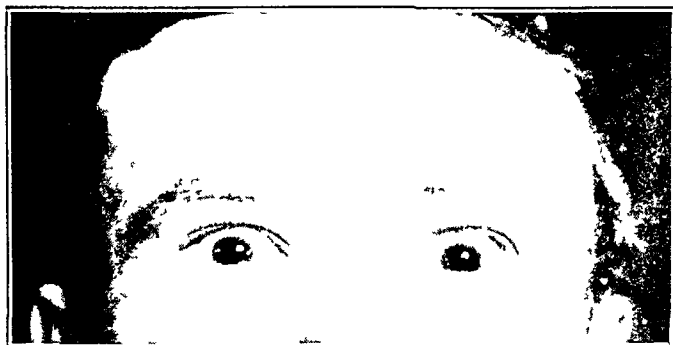


Fig 4—Marked widening of the palpebral aperture, which produced increased intraocular pressure

Attention should be called to an occasional rise in intraocular pressure dependent on the mechanical pressure of the upper lid on the globe. In 2 cases observed the exophthalmos was minimal, but the contraction of Muller's muscle in the upper lid was pronounced. Tonometric readings varied from 35 to 40 mm of mercury (Schiotz). There was no field defect or evidence of glaucoma. This condition needs no ocular treatment per se and is comparable in reverse to the

lowered intraocular pressure in the eye on the side of a unilateral peripheral facial paralysis as compared with the pressure in the sound eye (fig 4)

The inhibiting action of thyroid secretion on the development of exophthalmos is further emphasized by the aggravation of the exophthalmos (thyrotropic type) after thyroidectomy, producing the so-called malignant type of exophthalmos and frequently necessitating the Naffziger operation in order to preserve vision. The value of the operation is well exemplified by case 4, in which the exophthalmos receded from 33 to 18 mm. The importance of uncapping the optic foramen is also stressed.

CASE 4—M. J., a woman aged 34, underwent a subtotal thyroidectomy in March 1943. There is no record of exophthalmometric measurements previous to operation. Her basal metabolism before operation was 25 per cent above the average normal.

When she was first seen, on April 21, 1944, she stated that after the birth of a child two years and four months before she began to have "thyroid trouble." The exophthalmos began to increase two months after the operation.

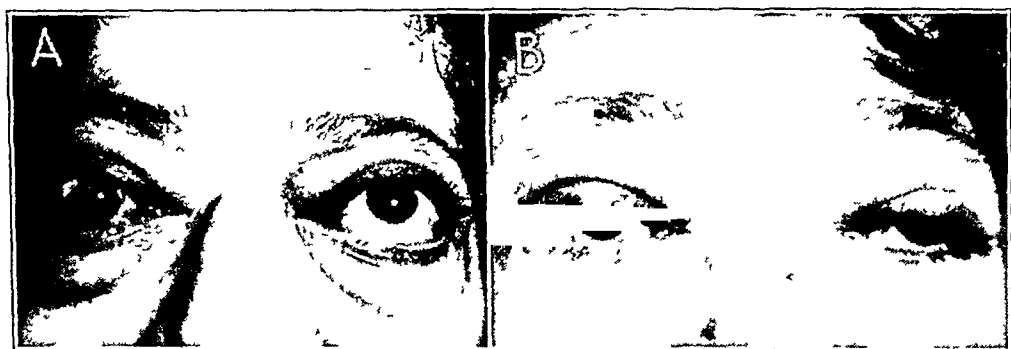


Fig 5 (case 4)—A, patient before a Naffziger operation was undertaken, showing the extreme left hypertropia, exophthalmos and venous congestion, B, appearance two months after operation.

On April 26, with the base line at 105 mm, her measurements were 32 mm in each eye. Vision could be corrected to 20/30 in the right eye and to 20/100 in the left eye. Her near point of convergence was 45 mm. There was a scleral exposure of 5 mm below the right cornea and of 4 mm below the left cornea. Edema of the lids was graded as 3 plus and chemosis of the right conjunctiva as 1 plus. There was limitation of movement of the lateral rectus muscles, being greater in the right eye than in the left eye. Intraocular tension was 20 mm in each eye. The fundus showed venous congestion of the retina. Thyroid substance was prescribed. Determinations of blood sugar and roentgenographic examination of the sella turcica were performed, the results of both being within normal limits. On July 14, the patient was taking 3 grains (195 mg) of thyroid U. S. P. daily. Her basal metabolism on April 27 was 1 per cent above the average normal.

On July 21, she reported that for the past week she had been seeing double. Paresis of the right inferior rectus muscle was present. Examination of the visual fields at this time showed a central scotoma for red in both eyes and

loss of the superior temporal field for red in the left eye. Her fields were normal for a 3 mm white test object at 330 mm and vision was 20/25 in the right eye and 20/200 — in the left eye. On July 28, vision had decreased to 20/70 in the right eye and to 20/200 in the left eye. Two roentgen treatments to the pituitary gland (40 r) were ordered, after which the patient became much worse, and on August 17, with a base line of 105 mm, her exophthalmos measured 33 mm in each eye. Vision was reduced to 6/200 in each eye. The fields now showed bitemporal contraction with a 3 mm white test object at 330 mm and a central scotoma in each eye for both color and form. Examination on August 21 disclosed paresis of the depressors of the left eye, producing left hyperphoria. Vision, however, was 20/200 in the right eye and 3/200 in the left eye, and the chemosis had somewhat lessened.

A Naffziger operation was performed on August 28. The surgeon reported that there was little orbital fat and that the ocular muscles showed marked hypertrophy and appeared thick and gray. Five weeks later, with a base line of 105 mm, her measurements were 24 mm in the right eye and 22 mm in the left eye. Pulsations could be noted in the exophthalmometer. Vision in the right eye was now 20/25+ with correction, and she read Jaeger type 1. The central scotoma had disappeared. There was still weakness of the right inferior and lateral rectus muscles. Corneal sensitivity was reduced in this eye. In the left eye, the field was much worse and vision was limited to perception of hand movements. Optic nerve atrophy could now be seen in this eye. Roentgenograms of the optic foramina disclosed removal of the upper part of the right optic foramen but a closed ring in the left foramen, a condition which may account for the absence of visual recovery in the left eye. The patient was under treatment with 4 grains (0.26 Gm) of thyroid given by mouth daily.

Her status at the time of this report shows that the exophthalmos has been further reduced to 18 mm, a total reduction of 15 mm from the preoperative measurements. Vision is 20/30 in the right eye and is limited to perception of hand movements in the left eye (fig 5).

An increase in the exophthalmos of hyperthyroidism may be related in part to such factors as security, frustration, violent emotional trauma and infection. Case 5 is illustrative.

CASE 5—T W, aged 42, had an only son who was a navigator in the air force. He was stationed near home and came in every week end. While home on furlough, he received word that he was about to be transferred south, from which point, of course, he was led to believe that he would be sent across shortly. The last day of the furlough found the worrisome mother with swollen upper eyelids. This was at the end of January 1944. We saw her first on Feb 8, 1944. With the exophthalmometer at 104 mm, her exophthalmos measured 20.5 mm in each eye. She had early signs of hyperthyroidism. One month later, with the same base line the measurements were 22.5 mm for each eye and on March 21 they were 23.5 for the right eye and 23 mm for the left eye. Her basal metabolic rate was +45 per cent (see case 3).

Bilateral paresis of the inferior oblique muscle is a rare complication following thyroidectomy in which, inadvertently, some of the parathyroid glands have been removed. No similar account could be found in the literature.

CASE 6—V C had a basal metabolic rate of 45 per cent above the average normal, with symptoms of hyperthyroidism. A subtotal thyroidectomy was done on June 7, 1944, after which paralysis of the vocal cords and tetany resulted. The ionized calcium fell to 3 mg (normal 4.8 to 6.3 mg) per hundred cubic centimeters. She complained of diplopia. Ophthalmologic examination disclosed bilateral paresis of the inferior oblique with pseudoptosis. Her measurements in the primary position at 13 inches (33 cm) were 4 Δ of esophoria and 5 Δ of right hyperphoria, and at 20 feet (6 meters), 7 Δ of esophoria and 1½ Δ of right hyperphoria. By December the squint had considerably improved, and her last examination, on Feb 7, 1945, showed orthophoria for distance and left hyperphoria of 2 Δ for the 13 inch distance. On looking up and to the right she had right hyperphoria of 4 Δ , and on looking up and to the left, left hyperphoria of 6 Δ , at 13 inches. No patch for the eye was necessary at this time.

Cataracts have frequently been described following tetany due to parathyroprivia, but a nuclear lesion such as must have been present in this case has not previously been described. The serum calcium of the patient is now normal. The patient was treated with calcium gluconate, preparations of vitamin D and dihydrotachysterol.

CONCLUSIONS

In 21 of 22 patients with hyperthyroidism, pupillographic examination revealed a redilation block. This is ascribed to a hypothalamic origin and lends the first tangible evidence to the confirmation of Marine's hypothesis.

In our hands, the administration of neostigmine bromide, a preparation of vitamin E and pyridoxine, failed to reduce exophthalmos.

The administration of iodine orally and pregnancy may occasionally result in regression of exophthalmos.

If vision is impaired because of involvement of the optic nerve in patients with thyrotropic exophthalmos, complete uncapping of the optic foramen should be included in the decompression.

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CYCLOPIA

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CYCLOPS is a fetal monstrosity with a single central eye. Some reports of this interesting anomaly have been made, but relatively few have included detailed studies of the eyes. Because of the interesting anomalies observed in 2 cases of cyclops, this report has been prepared. The bibliography was recently reviewed by Krafka¹ and Kindred,² and an extensive study was made by Adelman³. This malformation was described in the mythology of the ancient Greeks in a race of giants called cyclopes. They were destroyed by Apollo, who was angry at them for forging the thunderbolt that killed his son Aesculapius, the great physician.

Cyclopia is a congenital anomaly but is not hereditary, since life is impossible, in the usual case the child is born dead or dies soon after birth, so that no cyclops has ever reproduced. A familial incidence has not been reported, except by Klopstock⁴.

The development of cyclopia depends on local factors acting on the midline structures of the face at or before the time of development of the anlagen of the eyes. This has been demonstrated in the artificial production of cyclopia in lower forms by Dareste,⁵ in 1877, by Stockard,⁶ in 1909, by Loeb,⁷ in 1915, and by Mangold,⁸ in 1931.

The striking feature is the replacement of the normal two eyes by a single median eye. The nose is usually anomalous and is either

This work was done under the Wilham L. Hernstadt Fund at Montefiore Hospital for Chronic Diseases.

1 Krafka, J. Cyclopia and Arhinia. New Concept, Arch Ophth **33** 128 (Feb) 1945.

2 Kindred, J. E. Cyclopia Completa and Arhinocephalia Completa with Umbilical Hernia in a Full Term Child. Report of a Case, Arch Ophth **33** 217 (March) 1945.

3 Adelman, H. B. The Problem of Cyclopia, Quart Rev Biol **11** 161 and 284, 1936.

4 Klopstock, A. Familiares Vorkommen von Cyklopie und Arrhinen- cephalie, Monatschr f Geburtsh u Gynak **56** 59, 1921.

5 Dareste, C. Recherches sur la production artificielle des monstruosités, en essais de teratogenie experimentale, Paris, 1877.

6 Stockard, C. R. The Artificial Production of One Eyed Monsters and Other Defects Which Occur in Nature, by the Use of Chemicals, Anat Rec **3** 167, 1909.

absent or replaced by a proboscis-like structure located above the eye. The cyclopean eyes described in the literature were not all truly single eyes, as actually the single median eye is the rarest form, most of them were partially fused double eyes. One of my specimens had a perfect single eye, the other had a fused double eye. Both these specimens passed through several hands before reaching me, and I regret my inability to obtain any significant history.

DESCRIPTION OF SPECIMENS

CASE 1—This specimen was a true cyclops, with a single median eye located in the middle of a hideous face. The chin was very short and the upper lip



Fig 1—Cyclops with a single central eye, a proboscis above and no nose

unusually long, extending right up to the eye without any intervening nose. Above the eye was a strange-looking proboscis with a blind central opening, which was a vestigial nasal passage and in general resembled a pig's snout. The hair line came low down, close to the proboscis.

The hexagonal lid fissure was wide open, and the lid had insufficient tissue to draw over the eyes. The upper lid border was continuous. The lower lid border was interrupted in the middle and was replaced by a small conjunctival fold. The separation of the lower lid formed the only bilateral structure about this eye. There was no sign of any puncta or nasolacrimal passages. The cornea

7 Loeb, J. The Blindness of the Cave Fauna and the Artificial Production of Blind Fish Embryos by Heterogenous Hybridization by Low Temperatures, *Biol Bull* 29 50, 1915

8 Mangold, O. Das Determinationsproblem. III. Das Wirbeltierauge in der Entwicklung und Regeneration, *Ergebn d Biol* 7 193, 1931

was normal. The iris was short, stubby and rudimentary in development, with vascularized pupillary membranes bridging the pupillary zone. Some anomalous ciliary processes were observed on the posterior surface of the iris (fig 3).

The lens was normally developed, but around the lens was a cellular membrane with many thin-walled blood vessels, which connected with the pupillary membrane. This was the remains of the tunica vasculosa lentis, which normally appears for a period during fetal life and is often observed in premature infants.



Fig 2 (case 1) —Cyclopean eye $\times 8$

The retina was divided into two main zones, with notable differences between them. In the first zone there was well developed retina, with pigment epithelium and choroid beneath it. The second zone extended over a considerable area at the posterior pole and was characterized by absence of pigment epithelium and a conspicuous change in the choroid, which was replaced by a layer of delicate connective tissue with few vessels. The choriocapillaris and the lamina vitrea had disappeared where the pigment epithelium was absent. The retina associated with this area was poorly developed and had a small cellular content, no rods or cones and many irregular rosettes. Rosettes were present in both portions of the retina, but where the pigment epithelium and the normal choroid underlay the retina the rosettes were large and cellular and formed complete tubes, lined with five to ten cells. In the area without pigment epithelium and with a poorly developed choroid the rosettes were smaller, had fewer cells and did not form

complete tubes. In the periphery of the retina, especially in the superficial layers, were many cystic spaces. The rest of the retina presented many variations, one portion had the normal layers, while another contained many rosettes, which disturbed the orderly arrangement of the retina.

The rosettes were tubes formed by walls varying from five to ten cells in thickness, they were mainly circular, but many were longitudinal and some irregular. The rosettes were predominantly in the internal nuclear layer, and a few were present in the external nuclear layer. The part of the retina in which



Fig 3 (case 1)—Iris with pupillary membranes and tunica vasculosa lentis
× 38

rosettes formed in the external nuclear layer was further characterized by absence of rods and cones in the affected portions.

Rosettes were more numerous in the area without pigment epithelium and normal choroid, but there the cells forming their walls were only four to six cells deep and were not so tightly packed. Rosette formation has been found as a temporary phenomenon early in the human embryo and in the retina damaged by irradiation during fetal life, as reported by Goldstein and Wexler⁹. Another type of rosette is observed in retinoblastoma. Rosettes form as a result of an

⁹ Goldstein, I, and Wexler, D. Rosette Formation in Eyes of Irradiated Human Embryos, *Tr Am Acad Ophth* **35** 140, 1930



Fig 4 (case 1) —End of pigment epithelium on the left side of the figure, at this point there is a change in the choroid and retina, with disappearance of the choriocapillaris and the lamina vitrea $\times 65$



Fig 5 (case 1) —Tongue of anomalous retina growing beneath normal retina $\times 220$

excess of cells in the nuclear layers, with an infolding of the internal limiting membrane

Where the pigment epithelium was missing, there was a pronounced change in the choroid and retina. The choroid was replaced by a strand of delicate connective tissue, with few blood vessels and no choriocapillaris or lamina vitrea. The overlying retina had become anomalous and poorly developed, with many poorly formed rosettes and no rods or cones. My study and the investigations of others indicate the interdependence of the pigment epithelium and the choroid in their development. Some authors have suggested that the pigment epithelium dominates the development of the choroid. The absence of a good choroid secondarily affects the nutrition and development of the retina.

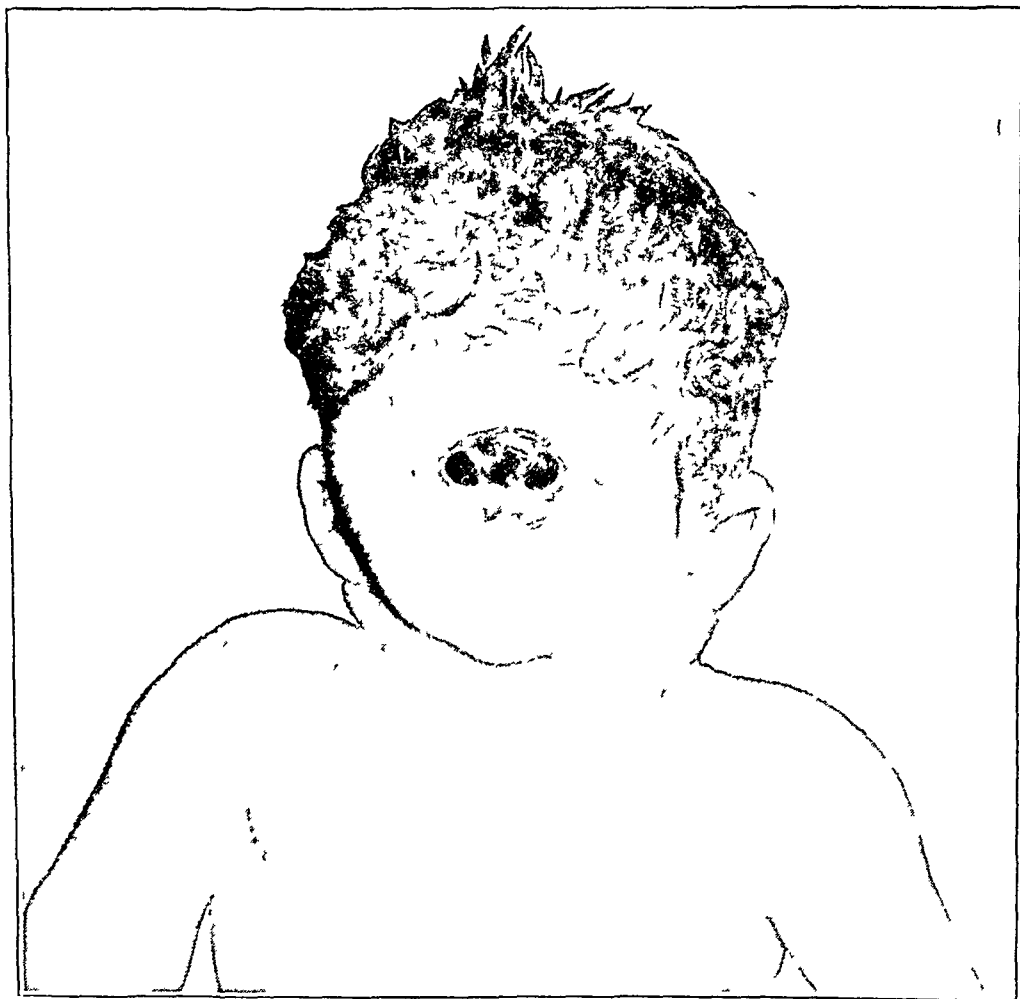


Fig 6 (case 2) —Cyclops

In another bizarre development (fig 5), a strip of anomalous retina grew beneath the rods and cones of the more orderly retina beside it.

CASE 2.—The two eyes were fused in one median structure, which was the outstanding feature of the face, as the other features were notable by their absence. There was no nose or mouth. The ears were deformed, they were placed low and curved down into the front of a very thick neck.

The lid fissure was elliptic except at the lateral ends, which came to a point, with a slight fold of the skin. There was a single continuous upper lid. The lower lid was interrupted in the center by a depressed zone, in the middle of which was a small elevation 15 mm in diameter, resembling a nipple.

The eyes were wide open, as the lids were retracted and underdeveloped for a fetus of the size of this specimen. The redundancy of lid tissue that permits easy closure was lacking, and there was no suggestion that these lids had been fused during fetal life. The edges of the lids were round, instead of presenting the

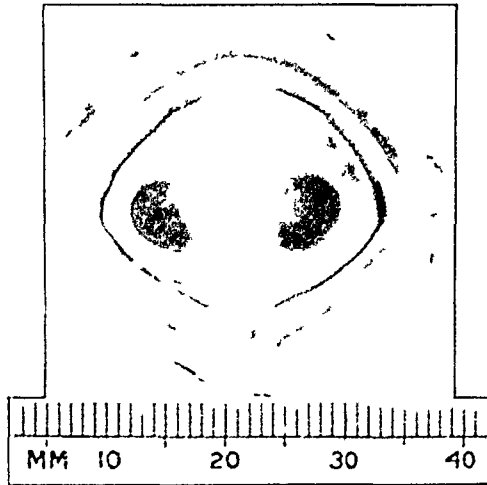


Fig 7 (case 2) —Cyclopean eye, showing two corneas, with a bridge of sclera between them



Fig 8 (case 2) —Section of the cyclopean eye, showing two corneas, with a bridge of sclera, two lenses, a deep pit at the optic disk and a single optic nerve $\times 5\frac{1}{2}$

usual flat end with square edges, and the sharp separation of the two portions of the lid by the gray line was lacking. The lid had many fine hairs, but no well developed eyelashes, at the margin. The normal meibomian glands, as well as the lacrimal gland and a strongly developed orbicularis muscle, were present. No evidence of puncta or lacrimal canaliculi was seen.

The orbit was a single cavity with a bony projection in the lower portion of the wall. In the depth of the orbit was a small central aperture for the single optic nerve. The optic foramen was a vertical oval, 1 mm wide and 2.5 mm high. On each side was the opening of the superior orbital fissure, 5 by 2 mm.

This cyclopean eye was a fused double eye, with two distinct corneas, separated by a bridge of sclera, two lenses, two retinas and a single optic nerve. The anterior view of the eye was almost circular, with a diameter of 21 mm. The eye was flattened anteroposteriorly, with a diameter of 10 mm.

The posterior view of the eye was unusual in that nine separate bands of muscle were attached to the globe, of which the lateral and the superior bands

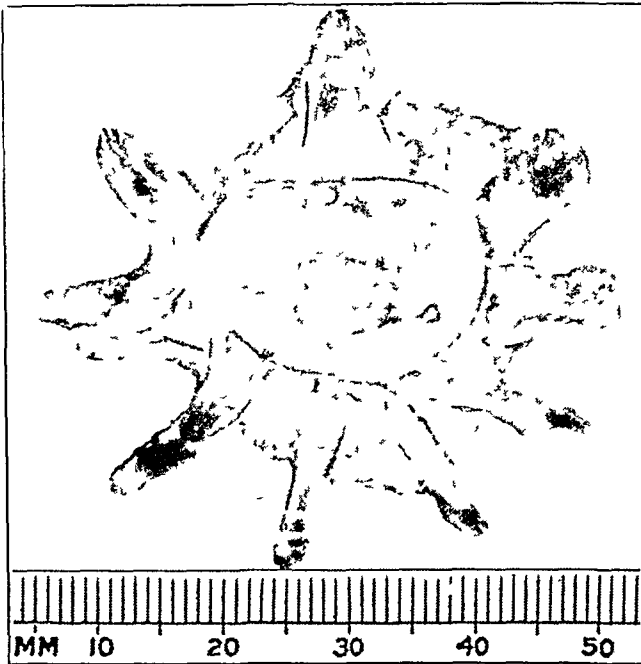


Fig 9 (case 2) —Posterior view, showing nine muscle bands attached to the eye

were best developed. All the muscles were attached on nearly one plane, slightly anterior to the equator of the globe. The optic nerve had a very broad attachment to the back of the eye, which tapered soon after leaving the globe.

The conjunctival fornix was shallow and began close to the limbus. On the lid the conjunctiva was one to two layers thick, in the fornix it was about five layers thick, and on the cornea and the sclera it was five to seven layers thick.

The two corneas were similar and very small, being 5 mm in diameter, they were avascular and separated by 7 mm of vascularized sclera. At the limbus blood vessels were seen in all layers, being most numerous near the surface. Schlemm's canal was not clearly defined, but there were small vessels filled with blood in the region usually occupied by this canal.

The space between the two corneas was bridged by the sclera, which presented an unusual inward projection of dense connective tissue, as shown in figure 8. Part of this elevation was covered with a rudimentary ciliary body and iris. This projection formed a partial separation between the fused portions of the two eyes.

Behind one cornea was a well developed iris with a central pupil. Behind the other cornea the iris was developed temporally, while on the medial side there was a coloboma, with only a rudimentary iris and ciliary body. The iris had loose connective tissue and many medium-sized blood vessels with very thin walls. The layer of spindle cells was not entirely flat but sent irregular branching formation into the iris. The two pigment layers of the iris were partially separated. The pectinate ligament was well formed where the iris was well developed and was missing where the iris was rudimentary. The pupils were bridged by delicate strands of pupillary membrane. The ciliary muscles were well developed except in the area of the coloboma of the iris, where they were represented by only a few isolated strands of muscle.

The pigment epithelium appeared normal over most of the eye but was missing in some areas. Where it failed to appear the adjacent choroid was

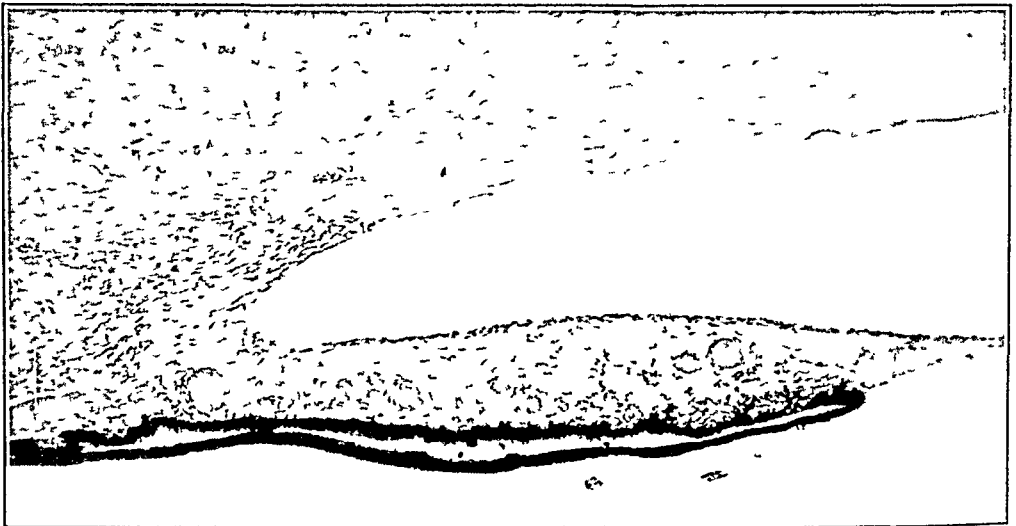


Fig 10 (case 2) —Iris, showing separation of the pigment layers and pupillary membranes $\times 78$

scantily developed, the choriocapillaris and the lamina vitrea were absent, and the overlying retina was poorly developed. This was true except in one area, which will now be described.

The choroid presented an unusual feature in the presence within it of a misplaced island of a retinal type of tissue, beneath the normal retinal layer. This was located near the colobomatous disk and consisted of typical layers of retinal elements and a few rosettes, as shown in figure 11. This remarkable and rare anomaly was described by Coats,¹⁰ who cited a few cases reported by Raab, in 1878, by Deutschmann, in 1881, and by Kundrat, in 1885. This island of retina was buried in the choroid and extended into the sclera. It contained only a few small vessels. Over most of it the pigment epithelium was absent, as well as the lamina vitrea and the choriocapillaris. The true retina above this area was relatively normal except that where the pigment epithelium was lacking there was an absence of rods and cones. The retinal cells in the mis-

10 Coats, B. On the Occurrence of Misplaced Derivatives of the Secondary Optic Vesicle in Congenitally Abnormal Eyes, *Ophthalmoscope* 7 724, 1909



Fig 11 (case 2) —Island of a retinal type of tissue buried in the choroid and sclera, with absence of the overlying pigment epithelium and a relatively normal retina above $\times 56$



Fig 12 (case 2) —Edge of the retinal island, showing an overlying layer of pigment epithelium with scant pigmentation $\times 77$

placed island were arranged in small layers and rosettes, but no rods, cones or nerve fibers were observed

Adjacent sections presented other developmental abnormalities which suggest a clue to the nature of this anomaly. As noted before, the pigment epithelium was absent over most of this area. Near the edge of the misplaced island of retina the pigment epithelium reappeared, at first as a nonpigmented, single layer of cells, then succeeding sections showed a thickening of the pigment epithelium, up to seven cells, with scanty pigmentation. The evidence was strongly in support of Coats's theory that the island of retina in the choroid is the result of a metaplastic development of the pigment epithelium, which, like the retina, is neurogenic. The explanation is theoretic but seems plausible.



Fig 13 (case 2) —Pigment epithelium elevated into many layers near the retinal island $\times 31$

The retina in the preparation was somewhat distorted, but there evidently were two complete retinas. The two layers of retina in the center had been somewhat disturbed in the preparation of the specimen. Other cases of cyclops with a single scleral cavity and two retinas, similar to this one, have been reported.

The retina for the most part was developed in a normal fashion except for a paucity of ganglion cells, and these were small, there were a few nerve fibers. Also, there were a number of areas with rosettes, apparently derived from cells of the internal nuclear layer. The rosettes rarely occurred singly but tended to appear in groups of two to five in any one section. When they appeared, they encroached on the neighboring layers and thickened the retina.

In those areas in which the pigment epithelium was lacking the rods and cones were absent, even when the rest of the retina was normally developed.

There were many fresh hemorrhages in the retina, which were probably the result of birth trauma and were similar to the hemorrhages often seen in the newborn.

The region of the disk had a deep, wide excavation, which had the shape of a flask, with a narrow opening. The pit was 3 mm deep, 4.5 mm at its widest part and 2 mm at its neck. Extending into its walls was a continuation of choroidal and retinal structures, which had undergone degeneration or maldevelopment. In the deeper part a thin bundle of atrophic nerve fibers appeared.

SUMMARY

Two cases of cyclops are reported. In 1 case the eye was a true single median eye, in the other, a fused double eye. Both were located in the center of the forehead and presented interesting anomalies.

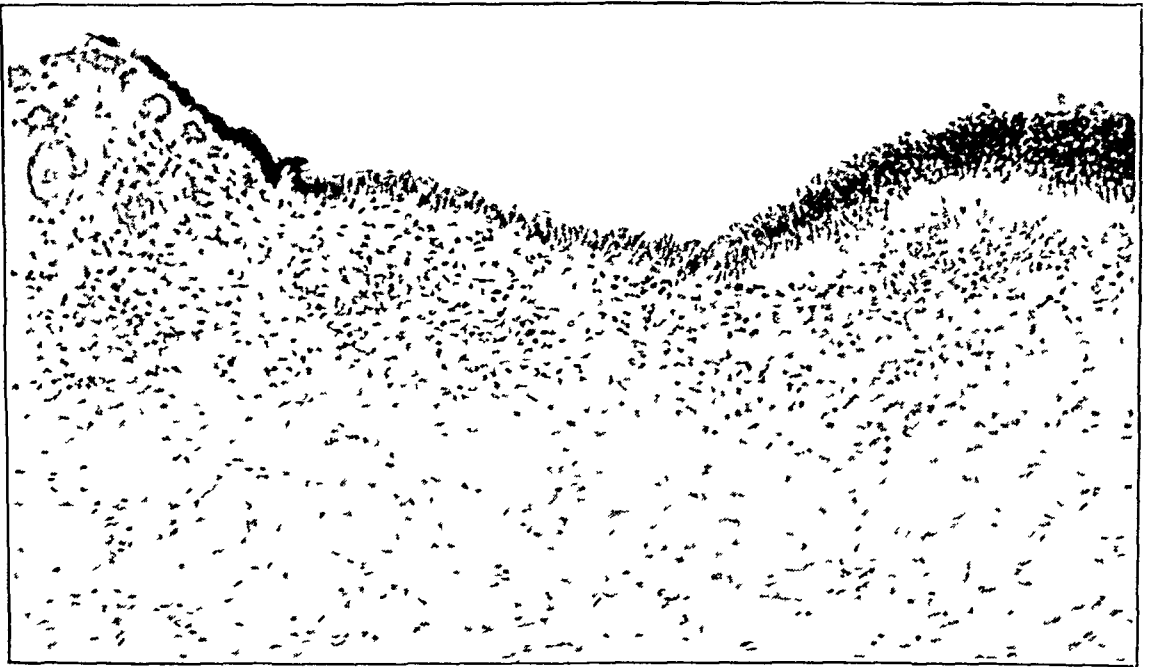


Fig 14 (case 2)—Higher magnification of a portion of figure 13, showing layers of pigment epithelium with scant pigmentation. $\times 70$

The importance of the pigment epithelium in the development of the choroid, as well as its influence on the retina, is indicated by this study.

In both cases the absence of pigment epithelium was associated with almost complete absence of the choroid, the choriocapillaris and the lamina vitrea and by maldevelopment of the overlying retina.

In 1 case a misplaced island of retina was observed buried in the choroid and sclera, in an area where pigment epithelium was lacking. Some proof was found that this anomaly was due to metaplastic development of the pigment epithelium into a retinal type of structure.

Dr B S Kramer and Dr M Chamlin furnished these specimens, and Miss Hilda Bergen made the microscopic preparations.

Obituaries

ROBERT K LAMBERT, M D

1898-1946

In the untimely death of Dr Robert K Lambert, at the age of 47, an inspiring colleague and a treasured friend was lost. He was born in New York city, with a distinguished background. His father was a brilliant physician and his mother a gifted musician. Music and painting became his hobbies. His devoted wife, Gerda, and his daughter, Patricia, survive him.

At Columbia University, Professor MacGiegor excited Dr Lambert's interest in the biologic sciences. After receiving the degree of Bachelor of Arts in 1918, he attended the College of Physicians and Surgeons and obtained his degree of Doctor of Medicine in 1922. After a two year internship in medicine at Mount Sinai Hospital, he sailed for London for a year of study and research under the famous physiologist, Prof Ernest Starling. On his return to New York, he engaged in general practice and taught physiology at Columbia University. He began his ophthalmologic career in 1928 with a residency in ophthalmology at Mount Sinai Hospital under Dr Julius Wolff.

He was awarded the DuBois Fellowship at the Presbyterian Hospital Institute of Ophthalmology, where he served for two years under Dr John M Wheeler, who had recently become professor of ophthalmology.

Dr Lambert spent five years in the New York Eye and Ear Infirmary, where he became assistant surgeon in the clinic of Dr Clyde E McDannald. His association with Montefiore Hospital began in 1933, by 1940 he was an attending, and at the time of his death consulting, ophthalmic surgeon. Montefiore Hospital is greatly indebted to him for developing the ophthalmic department and founding a laboratory for research.

His affiliation with Mount Sinai Hospital was maintained for almost a quarter of a century, from his internship, in 1922, until his death. In 1943 he was appointed attending ophthalmologist to Mount Sinai Hospital.

His pleasant personality and vigorous leadership enriched the scientific achievements of the hospitals he served.

Read at the meeting of the New York Academy of Medicine, Section of Ophthalmology, Dec 16, 1946

In 1945 he was appointed clinical professor of ophthalmology at the College of Physicians and Surgeons

He was a fellow of the New York Academy of Medicine and served as secretary of its Section of Ophthalmology in 1939. He was a fellow of the American College of Surgeons and the American Academy of



ROBERT K LAMBERT, MD

1898-1946

Ophthalmology and Otolaryngology. He was a member of the Association for Research in Ophthalmology, Inc., and the American Association for Advancement in Science.

The end of World War I found him a private in the Army in the S A T C. In World War II he was commissioned a major in the Medical Corps of the Army and served until his health failed.

Although the last year of his life was clouded by the knowledge of his destiny, he spent it without bitterness in hard work and deep study

Dr Lambert's ophthalmologic career was based on a broad training in medicine and ophthalmology and was stimulated by his interest in research. Only a portion of his research work was recorded in the seventeen papers he published. His great joy was to guide the men on his staff to research work, in which he gave them the best of training. For that purpose he devoted a good deal of his time, energy and funds. His most enduring memorial will be the strong impression he left on those who worked with him as they hope to carry on in his tradition. A hard worker and a diligent student, he accomplished a great deal in a short lifetime and died at the height of his career, while at the threshold of greater promise.

SAMUEL GARTNER, M D

News and Notes

EDITED BY DR W L BENEDICT

GENERAL NEWS

Graduate Course of the Gill Memorial Eye, Ear and Throat Hospital.—The twentieth annual spring graduate course of the Gill Memorial Eye, Ear and Throat Hospital will be held at Roanoke, Va, on April 7 to 12, 1947. One of the guests of honor, Dr A J Ballantyne, Glasgow, Scotland, will speak on April 7, at 8 p m, on "Clinical Research and Medical Practice." The regular sessions on the eye will be held on April 10 to 12, and the list of speakers is as follows:

Dr Eugene M Blake "Pathology of Glaucoma," "Choice of Operations in Glaucoma," "Unilateral Exophthalmos," "Fundus Changes in Blood Dyscrasias."

Dr William T Hunt "Essential Points in Routine Refraction," "Ocular Therapeutics," "Management of Cases of Lateral 'Phoria' and 'Tropia,'" "The Near Point Examination."

Dr Arthur J Bedell "Retinopathy of Hypertension," "Fundus Changes in Myopia," "Anomalies of the Fundus," "Differential Diagnosis of Optic Neuritis from Papilledema."

Dr A J Ballantyne "The Ocular Manifestations of Diabetes Mellitus," "Injuries of the Eye by Blunt Objects," "Birth Injuries of the Eye," "Some Intractable Diseases of the Cornea and Conjunctiva," "The Etiology and Differential Diagnosis of Rapid Loss of Vision," "The Nonsurgical Treatment of Cataract and of the Cataract Patient."

Dr R Townley Paton "Corneal Surgery, with Particular Reference to Corneal Transplant."

Dr E G Gill "Surgery of the Eye."

Dr William P Beethan "Surgery of the Eye," "Diabetic Retinopathy," "The Management of Some of the External Diseases of the Eye," "Keratoconjunctivitis Sicca," "Crystalline Lens in Diabetes."

Dr Bernard Samuels "Histology of the Eyeball, with Special Reference to Inflammation and Surgery."

Dr Raymond E Meek "Detachment of the Retina and the Surgical Treatment," "Minor Surgery of the Eyelids and Conjunctiva," "Cataract Extraction," "The Surgical Management of Crossed Eyes."

Annual Postgraduate Course in Ophthalmology and Otolaryngology.—The thirteenth annual postgraduate course in ophthalmology and otolaryngology was given in Charlottesville, Va, Dec 9 to 12, 1946. The lectures and clinics were held in the amphitheater of the University of Virginia Department of Medicine.

The lecturers and the subjects were as follows

Dr Bernard Samuels, assisted by Dr E Buichell "Sympathetic Ophthalmitis and Tuberculosis of the Globe, Pathologic Conditions of the Fundus Seen with the Ophthalmoscope, Perforating Wounds of the Globe"

Dr Alan C Woods "Ocular Manifestations of Congenital Syphilis, Ocular Manifestations of Acquired Syphilis, Ocular Brucellosis"

Dr A D Ruedemann "Surgical Correction of Eye Muscle Errors, Treatment of Cataract, Full Eye Plastic Implant"

Dr S Judd Beach "Hysterical Amblyopia with Reference to Confused Diagnosis, Routine Examination of the Eye, Refraction"

Sanford R Gifford Memorial Lecture—The third annual Sanford R Gifford Memorial Lecture was given at the Murphy Memorial Auditorium, 54 East Erie Street, Chicago, on Jan 20, 1947, by Dr Frederick C Cordes, of San Francisco The title of his address was "Types of Congenital Cataract"

SOCIETY NEWS

Association for Research in Ophthalmology—The next meeting of the Association for Research in Ophthalmology will be held in the auditorium of the Atlantic City Junior High School, Ohio and Pacific Avenues, Atlantic City, N J, entrance on Pacific Avenue, on Tuesday, June 10, 1947

Washington, D C, Ophthalmological Society—The Washington, D C, Ophthalmological Society held its regular meeting on Monday, Jan 6, 1947, at the District of Columbia Medical Society Building, Washington, D C

The guest speaker for the evening was Dr Charles E Iliff, of the Wilmer Ophthalmological Institute, Johns Hopkins University His subject was "Beta Irradiation in Ophthalmology"

A case presentation was given by Dr M Noel Stow on "Pseudo-xanthoma Elasticum with Angioid Streaks The Syndrome of Gronblad and Standberg," and 2 case presentations were made by Dr Ralph N Greene Jr, 1 on "Possible Tumor of the Macula" and the other on "Multiple Cholesterol Deposits in the Retina" Dr Edward J Cummings spoke on "Epithelioma of the Lid," and Dr A J Delaney, on "Pigment Proliferation in Benign Melanoma"

The meeting was then adjourned until February 3, when a special meeting is to be held with the W Thornwall Davis Post-Graduate Course in Ophthalmology (George Washington University School of Medicine)

Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Blind

THE INCIDENCE AND CAUSES OF BLINDNESS IN THE BRITISH COMMONWEALTH ARNOLD SORSBY, Brit M J 2:557 (Oct 27) 1945

This paper is the report of a painstaking and laborious investigation to determine the number of blind persons, the causes of blindness and the prevention of blindness in the British Commonwealth. The article cannot well be abstracted and should be read in the original. A summary follows.

The number of blind in the British Isles is not less than 90,000 and is likely to exceed 100,000. In the white population of the Dominions it is between 40,000 and 50,000. In the native population of the British possessions in Africa, Asia and Indonesia it is considerably more than 10,000,000. There has been a marked decline in the incidence of blindness in childhood in England and Wales during the past twenty-one years, but there is no evidence that there has been any substantial decrease in the older age group. Before long the decline in the incidence of blindness in childhood will come to an end, as already about 65 per cent of all blindness in children is due to congenital and genetic defects, not readily amenable to treatment. With the rapid elimination of blindness due to infectious disease, intensive research in the problems of genetic disease, maternally transmitted infections, cataract, glaucoma and the pathology of senescence has become an immediate task if the incidence of blindness in England and Wales is to be reduced. In the native population of the British possessions the incidence of blindness could be reduced immediately and effectively by the organization of facilities for the intensive exploitation of the sulfonamide compounds and penicillin in the treatment of the widely prevalent ocular infections.

ARNOLD KNAPP

Conjunctiva

A CORNEAL GRAFT OPERATION FOR RECURRENT PTERYGIUM J L REIS, Brit J Ophth 29:637 (Dec) 1945

In cases of recurrent pterygium Reis first does a modified McReynolds operation. A superficial corneal layer is then obtained from an enucleated eyeball. The graft is dissected after its margins have been delineated by two parallel, superficial incisions. The size of the graft depends on the extent of the denuded cornea to be covered and will, therefore, vary from 3 to 5 mm. The graft is transferred on the knife blade and slid onto the cornea of the recipient. Then the conjunctival flap is raised slightly with opened forceps and the graft is slid underneath. It is not essential that the conjunctival flap should cover the whole of

the corneal graft The eye is dressed with calcium penicillin-sulfathiazole powder dusted into the conjunctival sac

The article is illustrated

W ZENTMAYER

Cornea and Sclera

DENDRITIC KERATITIS ASSOCIATED WITH CHRONIC MALARIA R D HARLEY and R F KAISER, *Am J Ophth* 28: 1309 (Dec) 1945

Harley and Kaiser stress the importance of dendritic keratitis as a diagnostic indication of malaria and report 3 cases in which the plasmodium was found

W S REESE

ANATOMIC CLASSIFICATION OF FAMILIAL CORNEAL DYSTROPHIES A FRANCESHETTI and J BABEL, *Ophthalmologica* 109 169 (April-May) 1945

Histologic studies in 14 cases of corneal dystrophy are reported, and on this basis a classification of corneal dystrophies is presented Two main types can be distinguished 1 The progressive, noncongenital form, with two main subtypes (a) The "crumb-lace" type characterized by hyaline degeneration of the corneal epithelium and the deposition of a hyaline, basophilic material under the epithelium In the "lace" type the changes in the cornea are somewhat coarser and deeper than in the "crumb" type (b) A recessive, spotty type, in which all the corneal cells (epithelium, substantia propria and endothelium) show a deposition of granular albuminous material, in addition to the hyaline degeneration 2 The comparatively stationary, congenital form In this form no degeneration is present, but the layers are separated with distribution of a granular substance (lipid?) in the cells of the stroma The inheritance is generally recessive in these cases, and the changes in the corneas resemble, both clinically and histologically, the alterations in the corneas in lipochondrodystrophy

F H ADLER

HERPETIC KERATITIS A LABOR ACCIDENT J SELLAS and J CASANOVAS, *Arch Soc oftal hispano-am* 4: 262 (April) 1945

The authors accept the traumatic origin of herpetic keratitis, in their experience, however, it seldom occurs Among 20,000 cases of industrial injury to the eye only 6 instances have been recorded They describe these cases and discuss Grutter's views with respect to trauma as an etiologic factor in this condition The authors express the opinion that if herpetic lesions appear in less than two days after the alleged injury they should not be considered of traumatic origin If the lesions make their appearance a week after the accident, all circumstances present should be evaluated If proved serious ocular trouble develops during the period between the date of the accident and the day on which the diagnosis of herpes is made, the case should preferably be accepted as of traumatic origin

H F CARRASQUILLO

General

STATISTICAL ANALYSIS OF 1,000 CONSECUTIVE NEW EYE PATIENTS
A DEROTH, *Am J Ophth* 28:1329 (Dec) 1945

This analysis is concerned mainly with refraction, the findings indicating the superior skill of ophthalmologists over optometrists and the necessity for examination of the eye by a physician

W S REESE

BIOMICROSCOPY OF THE EYES IN EVALUATION OF NUTRITIONAL STATUS
CORNEAL VASCULARIZATION R K ANDERSON and D F MILAM,
J Nutrition 30:17 (July) 1945

In a survey of the nutritional status of a rather large population group, no correlation could be found between corneal invasion and the level of riboflavin in the diet. There was also no correlation with other signs suggestive of riboflavin deficiency.

Corneal invasion was found to be much more frequent in the white race than in the Negro race.

W ZENTMAYER

General Diseases

OCULAR FINDINGS IN TROPICAL TYPHUS (TSUTSUGAMUSHI OR
JAPANESE RIVER FEVER) E A DONEGAN, *Brit J Ophth* 30:11
(Jan) 1946

A total of 101 cases of tropical typhus are described with respect to their salient features. Four of these were fatal. In the acute stage there was conjunctival hyperemia. The optic disk showed hyperemia, with an overlying central haze in the vitreous and blurring of the margins of the disk, often accompanied with swelling of the disk. While haze in the vitreous, taken as a more reliable sign of optic disturbance, occurred in 32 cases, only 2 cases of atrophy of the optic nerve were seen, in 1 of which the serum gave a strongly positive Kahn reaction. In many cases signs of descending neuritis, as described by von Graefe, were present. The signs disappeared without any residual damage to the optic nerve of the retina.

The interpretation placed on the ocular signs is that of a vascular upset, and not of neural or neurologic involvement through invasion of the nerve tissues by the rickettsial bodies.

W ZENTMAYER

TEMPORARY CATARACTS IN DIABETES R D LAWRENCE, *Brit J Ophth*
30:78 (Feb) 1946

Lawrence observed 2 patients with diabetes in whom cataracts were seen both to form and to clear up in a previously normal lens. Both patients were myopic but had otherwise normal eyes when first seen for diabetes. Both had high blood sugar but no ketosis or signs of body dehydration. In both cataract developed at a stage of much improvement in the diabetes. In the first patient the cataracts first appeared about the sixteenth day of treatment with insulin and lasted three weeks. The cataracts of the 2 patients were similar in their dark rosette appearance and in occupying the central portion and the upper

quadrant of the lens. As these cataracts can be produced both by severe diabetes and by its treatment, the only common causal factor that suggests itself to the author is a change in hydration, both dehydration in progressively increasing diabetes and rehydration under treatment. The literature is reviewed. The article is illustrated.

W ZENTMAYER

BILATERAL OPTIC ATROPHY AS A SEQUELA TO THROMBOCYTOPENIC PURPURA P V CARRELI and J P CANGELOSI, J A M A 129 550 (Oct 20) 1945

A boy aged 6 years had uncontrollable epistaxis following an infection of the upper respiratory tract. A diagnosis of purpura hemorrhagica following infection of the upper respiratory tract was made. During the second week of hospitalization sudden blindness occurred. There was doubtful light perception in both eyes. The pupil was dilated and did not react to stimulation with light. Examination of the right eye showed ecchymotic spots on the lids, slight exophthalmos and limitation of ocular movements. In the left eye there were a staining infiltrate of the cornea at 5 o'clock and slight blurring of the margins of the optic disk with a retinal hemorrhage. A splenectomy was done. The liver was large. The child continued to improve, and when she was last examined there was bilateral atrophy of the optic nerve with doubtful light perception. The authors consider the case of interest because of the rare occurrence of bilateral atrophy of the optic nerve as a sequel to thrombopenic purpura. Splenectomy performed during the quiescent stage of the disease produced almost immediate return of the blood picture to normal, and the ocular condition is still unchanged twenty months after the onset of the disease.

W ZENTMAYER

Hygiene, Sociology, Education and History

GRADUATE TRAINING IN OPHTHALMOLOGY H S GRADLE, Am J Ophth 29:24 (Jan) 1946

Gradle gives a brief history of graduate training in ophthalmology in the United States and pleads for a "third level" of university training, particularly as it pertains to medicine and the medical specialties. This level should cover the period between completion of the general internship and the completion of training required by the special boards. This gap should be filled under university jurisdiction, and a certain degree of uniformity in ophthalmic training on a nationwide basis should be introduced.

W ZENTMAYER

Injuries

WAR SURGERY OF THE EYE IN FORWARD AREAS E C ZORAB, Brit J Ophth 29:579 (Nov) 1945

The working of the ophthalmic unit is described. The method of choice for induction of anesthesia was continuous pentothal drip com-

bined with instillation of cocaine drops in the eye, morphine and scopolamine premedication and continuous administration of oxygen via an intranasal pharyngeal tube

Perforating wounds of the globe were the commonest type of injury requiring surgical treatment. Those produced by foreign bodies composed the majority. Analysis of the major operations performed during a year in the forward areas is given in detail, showing the relative frequency of various types of ocular injuries. The surgical procedures adopted in dealing with various ocular injuries are outlined.

W ZENTMAYER

OPHTHALMOLOGY IN THE BRITISH NORTH AFRICAN AND CENTRAL MEDITERRANEAN FORCES B W RYCROFT, Brit J Ophth 29: 594 (Nov) 1945

This account of the ophthalmic services of the British forces in the Western Mediterranean Theater covers a period extending from November 1942 to November 1944 and includes the campaigns in North Africa, Sicily and Italy.

The article is difficult to abstract. In the treatment of the socket, the use of firm petrolatum packs was thoroughly discouraged, but the elevation of the upper lid by straps of adhesive plaster so as to allow air to circulate within the socket represented an advance in ophthalmic treatment. It was essential in the early stages in cases in which the lid and orbit were wounded to separate the raw surfaces by a strip of petrolatum gauze, otherwise, lid and socket became firmly adherent by the time the patient reached a base hospital.

Except in cases of severe injury, corneal abrasions or ulcer, it is rarely necessary to tie up an eye, flaps or dark spectacles are preferable. When in doubt use a flap.

With all penetrating wounds of the eye the giant magnet is used as soon as possible after the injury. For localization the equatorial ring method serves most purposes.

The Lister frill excision is used for disorganized eyes when seen at an early stage, and at later stages an enucleation, with implantation of a 14 mm Perspex globe in Tenon's capsule, is carried out. The old evisceration operation is practically never done, and the usual method of enucleation alone is becoming infrequent.

W ZENTMAYER

EXPERIENCES WITH THE GIANT MAGNET AND METALLIC INTRAOCULAR FOREIGN BODIES IN RECENT BATTLE CASUALTIES R E WRIGHT and H A G DUNCAN, Brit M J 2: 658 (Nov 18) 1944

This is a report of observations showing that the intermittent application of the giant magnet at a number of sittings succeeded in moving a feebly magnetic particle. The authors note that a small magnetic foreign body or a larger feebly magnetic particle may behave as a nonmetallic body for a considerable number of applications and be labeled as such. From the case reported the following lessons are deduced. The posterior route is usually the best for foreign bodies situated in the posterior segment. The shortest route to the exterior is probably the best unless this drags the particle through a structure of greater importance than the one in which it is lodged. To work well

behind the equator, a beak-shaped magnet terminal is essential. The removal of small metallic intraocular foreign bodies of feeble magnetism depends on the patience and perseverance of operator and patient. It is important to remember that the frequent applications of the giant magnet increases the magnetism of feebly magnetic alloys. The application of a surface diathermy terminal to the sclera in the neighborhood of the metallic intraocular foreign body is likely to produce an uncontrollable reaction, so it is better to apply diathermy to the neighborhood of the scleral wound after the foreign body has been extracted.

ARNOLD KNAPP

MANAGEMENT OF INCREASED INTRAOCULAR PRESSURE FOLLOWING WAR TRAUMA (SECOND COMMUNICATION) S. KALFA, *Vestnik oftal* 24 55, 1945

When glaucoma is a result of anterior synechia, surgical intervention should be early in order to prevent permanent adhesions of the angle of the anterior chamber. The prolapsed iris should be excised and the wound covered after the method of Kuhnt for prevention of infection. The best measure of combating this type of glaucoma is Filatov's operation, "iridectomy duplex," which consists in a double incision of the cornea at the base of the synechia with the Graefe knife. A double iridectomy is done at these places. If the anterior chamber is shallow, an iridectomy ab externo is preferred.

The delay in restoration of the anterior chamber after injury is due either to fistula formation or to edema or hemorrhage in the vitreous. A prolonged delay in reformation of the chamber in the presence of an inflammatory process leads to formation of adhesions between the base of the iris and the cornea. The fistula should be closed after the method of Kuhnt, an iridectomy and cauterization of the edges of the fistula being done prior to it. If there is no fistula and the intraocular tension is increased, a posterior sclerectomy is performed with Elliot's trephine about 7 mm from the limbus, at the external margin of the superior rectus muscle. A bead of vitreous usually appears in the trephine hole, this is cut off with scissors. The anterior chamber is usually restored on the day following this procedure.

Extracapsular extraction leads to secondary glaucoma more frequently than intracapsular extraction, as the cortical masses may block the angle of the anterior chamber. Cyclodialysis is the method of choice.

Glaucoma after uveitis can be treated without operation, employing tissue therapy, miotics (with caution), mydriatics and retrobulbar injections of a 2 per cent solution of procaine hydrochloride. In cases of iris bombe or of occlusion of the pupil, transfixation of the iris after the method of Fuchs is recommended, as it causes little bleeding and the inflammatory symptoms are minimal.

O. SITCHEVSKA

Lens

CONGENITAL CATARACTS IN SISTERS WITH CONGENITAL ECTODERMAL DYSPLASIA H. N. COLE, H. K. GIFFEN, J. T. SIMMONS and G. M. STROUD III, *J. A. M. A.* 129:723 (Nov. 10) 1945

Two sisters aged 10 and 22 months, respectively, had congenital cataracts of the lamellar type, extreme internal strabismus, hypoplasia

of the nails, almost complete alopecia, atrophic nasal mucosa and generalized hypoplasia of the skin. Both children stood heat poorly, both were subnormal mentally, and the older had a dental hypoplasia. Microscopically there was an irregular hypoplasia of the skin and accessory structures—sweat and sebaceous glands and hair. In places all three were completely absent.

Involvement of all ectodermal elements as seen in these sisters is rare if not unique, and the picture presented approaches closely that of congenital ectodermal dysplasia of the anhidrotic type but perhaps would better be classified as a combined ectodermal dysplasia.

The dysplasia of ectodermal elements seen in these sisters with only a suggestive dental abnormality in the father and no other family history is probably "incompletely dominant" in type.

Simmons, in discussion, stated that it had been approximately one and one-half years since the cataracts were operated on. With corrective bifocal lenses, both children walked about freely, in contrast to their being content to sit still before. They recognized household articles and toys by name. The squint was unimproved.

The article is illustrated

W ZENTMAYER

COPPOCK CATARACT AND CATARACTA PULVERULENTA CENTRALIS
E ROSEN, Brit J Ophth 29: 641 (Dec) 1945

Rosen has made photographs with the slit lamp in 3 cases of Doyne's discoid cataract (Coppock). In the first case the opacity was seen to occupy the most central portion of the lens, its center being somewhat transparent. The cataractous disk was made up of tiny white, highly refractile, dotlike deposits, located in the fetal nucleus, with only the lucid interval separating the anterior and posterior portions. The Y sutures were in this same zone and could be made out more or less incompletely. The disk appeared to have a greater posterior than anterior bulge. In some of the spaces between the small white dots were areas which resembled the microscopic vacuoles seen in immature senile cataract. The appearance of the lens in the other 2 cases was similar to that in the first case.

W ZENTMAYER

DIABETIC NEEDLES E ROSEN, Brit J Ophth 29: 645 (Dec) 1945

Rosen describes a lenticular sign which he states has come to be known as the "diabetic needle," or "Roman numeral," sign, consisting of a spoke formation in the periphery of the lens. The needle appears as a linear black streak, no thicker centrally than it is peripherally. This is the most important feature, and even in cases in which there is adult spoke formation in the lens, characteristic of early change in senile cataract, there still may be superimposed on this cataract formation the characteristic "diabetic needle."

The sign is not constant, but when present it is specific for diabetes.

It is best observed when the pupil is dilated and the red reflex is studied with the (indirect) ophthalmoscopic method or with the retinoscope.

A brief résumé of the clinical history of 19 cases, with a drawing of the lenticular changes in each case, is given.

W ZENTMAYER

Neurology

POLYOPIA AND MONOCULAR DIPLOPIA OF CEREBRAL ORIGIN M B
BENDER, Arch Neurol & Psychiat 54. 323 (Nov-Dec) 1945

The author reviews the literature and discusses in a comprehensive and enlightening manner the factors giving rise to polyopia and monocular diplopia. He reports in detail 4 cases with the experiment and tests used to reveal polyopia and monocular diplopia. To quote directly

"The first 3 cases described show several things in common, namely, (a) scotomas in the fields of vision, (b) fluctuation, obscuration or extinction phenomena in the defective fields of vision, (c) disturbance in the mechanism of fixation, and (d) optical illusions. The fourth case is somewhat different, inasmuch as there were no demonstrable field defects and the double, or false, image was incomplete. Naturally, the first impulse is to attribute all these symptoms to a common cause, but this is possible only from the structural standpoint.

"One may safely assume that the scotomas were produced simply by damage to the calcarine cortex or the optic radiation. Here destruction of tissue produced absence of function. The rest of the symptoms, however, cannot be explained on a structural basis alone. They seem to be an expression of normal functions which become apparent only under pathologic conditions. Fluctuation, obscuration and extinction of visual perception are psychologic phenomena which become evident in patients with diseases of the visual cortex or pathways. This apparent disorder in perception is due to the presence, and not to a lack, of function.

"Disturbances in the mechanism of fixation, as noted in the cases described here, are also expressions of underlying normal functions which are thrown out of equilibrium.

"Fixation is maintained by a constant muscular effort in which the actions of all the ocular muscles are balanced. It is concluded that the rapid and involuntary movements of the eyes produced by faulty fixation tend to stimulate, simultaneously, the original macula and any new maculas which may have been formed as a result of impairment of vision."

S R IRVINE

A CASE OF OCCIPITAL LOBE INJURY J MACASKILL, Brit J Ophth 29
626 (Dec) 1945

A soldier aged 22 was hit on the right side of the back of the head by a bursting shell. Consciousness was never lost, but after the injury he could not see at all to the left side. One week later objects far out on the side could be seen but he was aware of a nonseeing area toward the center of vision. Three months later there was a healed, depressed wound in the occipital region to the right side of the midline. Both eyes were normal and had full vision. There was a left homonymous hemianoptic scotoma, with steep edges, but the fixation area was spared. The wound in the skull was opened and enlarged to expose healthy dura, the dural scar excised and bone fragment removed from the brain to a depth of 3 cm. The field defects indicated a lesion of the posterior part of the visual cortex mainly on the right side, and the findings at operation form a guide to their correlation.

The initial loss of the whole field on the left side resulted probably from a functional disturbance of all the right visual area of the brain at the time of the injury, and it may be noted that recovery commenced in that part of the field which corresponded to the region farthest from the injury. There was no opportunity to examine the field after operation, but the nature of the injury and the steep edges bounding the scotoma suggested that little, if any, improvement can be expected.

The article is illustrated

W ZENTMAYER

SIXTH-NERVE PARALYSIS AFTER SPINAL ANALGESIA W A FAIRCLOUGH, *Brit M J* 2:801 (Dec 8) 1945

After commenting on the scarcity of recent literature on this subject, the author reports that during the past two years he has observed 10 cases. He discusses various theories which have been advanced to account for this lesion and suggests a new theory, which, though not providing the basal cause of paralysis of the sixth nerve, would account for the fact that this nerve so frequently shows signs of injury earlier than any of the other cranial nerves, even without taking into consideration its anatomic disadvantages. The author first speaks of binocular vision and the necessary faculties which are concerned in its maintenance. From a phylogentic point of view, binocular stereoscopic single vision is one of the latest acquired attributes and probably is one of the first to be lost or disturbed under stress. Imbalance and insufficiencies of the ocular muscles, concomitant squint, heterophorias and refraction errors all have a definite bearing on the subject. The author suggests that the common presence of a defect in one or more of the conditions essential for the maintenance of binocular vision and an added toxin will together provide the factors producing the lesion of the abducens nerve.

In none of the 10 cases was the paralysis complete. A toxic drug acting on an unstable binocular function can very probably be the cause of the diplopia and paralysis of the abducens nerve following spinal analgesia. Thus, it will occur in a patient with esophoria, and the esophoria would become a manifest convergent squint with uncrossed double vision. Furthermore, the author thinks that no other theory has been put forward to account for the paralysis of the abducens nerve being so commonly unilateral and only partial.

Of the 10 patients reported on, 9 were examined after they stated that their eyes were again normal. Each showed a degree of esophoria, varying from 1 to 5 prism diopters at 6 meters, and none had exophoria.

The author then discusses the causal theories, the common symptoms, the prognosis and the treatment. The treatment is not very satisfactory, though the inhalation of oxygen has given definite relief in many cases.

During the period under review, spinal analgesia was administered to 2,021 patients, of whom 10 had paralysis of the sixth nerve. The author summarizes the condition as one which is founded on the instability of binocular vision.

ARNOLD KNAPP

BITEMPORAL HEMIANOPSIA DUE TO TRAUMA J BRENTA and P DANIS, *Ophthalmologica* 111.8 (Jan) 1946

Analysis of the cases already appearing in the literature and of a case in the authors' experience leads them to certain conclusions.

They believe that in some cases the direct mechanical effects of the trauma produce a sagittal tear of the chiasm, sometimes including neighboring structures, and that this is the direct cause of the hemianopsia. In other cases some secondary process must be added to the mechanical effects. In a third group of cases it is evident that there is no direct mechanical influence at all but that the hemianopsia is caused by a degeneration of fibers.

F H ADLER

Operations

FASICA-LATA TRANSPLANT FOR RETROTARSAL ATROPHY OF UPPER LID FOLLOWING ENUCLEATION N L CUTLER, *Am J Ophth* 29 176 (Feb) 1946

Cutler describes a procedure for restoring the normal fold of the upper lid after enucleation. He creates a tunnel below and following the curve of the brow, through which he pulls the shredded fascia lata. He has used this procedure with 134 patients.

W S REESE

TUBULAR STEM IN OPHTHALMOLOGY V FILATOV, *Indian J Ophth* 6 23 (July) 1945

The present article deals mainly with plastic operations using surface tissues and, principally, skin layers. Three fundamental principles of skin plastics are the Hindu method, the Italian method and plastic operations with unattached pieces of skin.

Filatov describes the method and technic of the tubular stem and states that it is a method and, as such, leaves scope for ingenuity of surgeons to devise the best method of achieving the required plastic result.

W ZENTMAYER

Orbit, Eyeball and Accessory Sinuses

EXPERIENCES WITH THE SURGERY OF THE ANOPHTHALMIC ORBIT A G DeVoe, *Am J Ophth* 28 1346 (Dec) 1945

DeVoe discusses surgery of the socket, especially operative methods for the deformity of sinking or retraction of the upper lid. He stresses the importance of cooperation of the artificial eye maker.

W S REESE

A CASE OF SIDEROSIS BULBI J E L BENDOR-SAMUEL, *Brit J Ophth* 30 85 (Feb) 1946

A man aged 35 complained of pain in an eye which had been blinded about a year before while he was firing a rifle at a "dead" grenade. The iris was discolored, and the cornea was edematous and infiltrated with spots of dark brown pigment. The lens was opaque. Vision was reduced to perception of light, and light projection was faulty. The tension was greatly increased. A roentgenogram showed the presence of an intraocular foreign body, this was removed through a scleral incision. About five weeks later a simple extraction of the cataract was carried out. One month later vision was 6/12. There were deposits of ferrous pigment on the posterior capsule. Discussion.

of the capsule was performed. The resulting visual acuity was 6/12. The visual field was considerably contracted. The case illustrates the value of surgical intervention for an eye with siderosis bulbi in an advanced state.

W. ZENTMAYER

SIDEROSIS BULBI. REPORT OF A CASE. A. PAULO FILHO, S. RAFAEL, SEBAS and A. GIARDULLI, Hospital, Rio de Janeiro 28: 339 (Sept) 1945.

A man harbored a chip of iron in his eyeball for eleven years before the appearance of siderosis bulbi. The cornea and muscular tissues of the iris did not contain iron pigment. The pigment was selectively located on the retina in the form of accumulations of free pigment in granulations. The iron in the eyeball was ionizable. Paulo Filho and his associates believe that the first change caused by metallic iron is the partial coagulation of the cytoplasm. Later the newly formed granulations of iron pigment cause necrosis of the retinal cells, with consequent blindness.

J. A. M. A. (W. ZENTMAYER)

Parasites

OCULAR CYSTICERCUS CELLULOSAE. REPORT OF A CASE OF PARASITE IN THE VITREOUS. C. COCKBURN, Brit J Ophth 30: 65 (Feb) 1946.

A man complained of a mist before the right eye. About six weeks later a well defined object shaped like a pear leaf with a stem that had a knob at the end like a serpent's head, which was constantly changing its position, was seen entoptically.

Ophthalmoscopic examination showed a ring of iris pigment on the anterior capsule of the lens, two lenticular opacities and vitreous haze with many dense, freely moving opacities in the vitreous. In the lower part of the vitreous there was a highly lustrous, almost completely spherical cyst, brilliant blue-green above, passing to a russet brown at the center and shading off to a lemon tint below. The upper periphery was surrounded by a narrow, brilliant golden halo. At the lower margin was the miniature tapeworm, constantly changing its position in a low, swaying movement. The head itself possessed power of movement. At the extreme periphery of the fundus was a large, irregular yellowish area, resembling acute choroiditis. The cyst was removed through a scleral incision. About ten months later the eye was quiet and had good light perception. The hooklets were those of *Taenia solium*. The article is illustrated.

W. ZENTMAYER

Society Transactions

EDITED BY DR W L BENEDICT

OXFORD OPHTHALMOLOGICAL CONGRESS REPORT OF THE THIRTY-SECOND ANNUAL CONGRESS AND A BRIEF HISTORY OF THE CONGRESS

Bernard Samuels, M D

New York ,

July 4-6, 1946

The thirty-second annual Oxford Ophthalmological Congress took place at Keble College, Oxford, England, on July 4, 5 and 6, 1946. Members of the congress, including lady members for the first time, were lodged under the hospitable roof of the college. The scientific proceedings, calling for thirteen papers and four demonstrations, were held in the nearby department of human anatomy, located in the museum of Oxford University.

On Wednesday evening, the third, an informal dinner was served in the Hall of the college, and for the convenience of those who could not arrive in time there was a buffet in the Junior Common Room (all places to older members as familiar as household rooms), where light refreshments were served. In this way, men eager to see one another, after the long war, were given a chance to renew friendships, and those come for the first time were requested to make their presence known to the honorary secretary.

On Thursday morning, the fourth, the day began at 7 30 with a bathing parade, which started at the porter's lodge at the college entrance for Parson's Pleasure, on the meandering, tree-arched Cherwell.

At 10 o'clock the scientific program began. The master, Mr Philip G Doyne, whose father had been the first to grace the chair, in a brief address bade the congress a cordial welcome. He called on Mr Philip Jameson-Evans to open a discussion on amblyopia. This was done under two headings: (1) toxic amblyopia and (2) congenital amblyopia. 1 The thesis was put forward that the toxicity of tobacco is dependent on a process of fermentation in the leaf, and emphasis was laid on the importance of the water content of tobacco and attention drawn to the effect that the metabolism of the liver has in toxic amblyopia. Alcohol and vitamin deficiency were mentioned as accessory factors. 2 The relationship of visual acuity, fusion, stereopsis and fields of vision was made clear, and electroencephalographic findings in cases of congenital nystagmus were correlated with present day theories of vision.

Dr Dorothy Campbell, the second speaker, restricted her discussion to primary amblyopia. Early amblyopia, congenital amblyopia and amblyopia ex anopsia were defined and critically differentiated from one another. Theories as to the causation of amblyopia were outlined, and methods of detecting and treating it in young children were described.

Mr Harold Ridley, the third speaker, based his discussion on an interesting series of cases of amblyopia from malnutrition, methyl alcohol and tryparsamide that came under his observation during service overseas

These three excellent and well delivered essays and the general discussion that followed completed the morning hours

After lunch the annual group photograph of the members of the congress was taken in "The Quad" of Keble College

The afternoon session began with a paper by Dr Bernard Samuels, entitled "Proliferation of the Epithelium of the Lens," in which were described changes in the epithelial system of the lens caused by lesions in other parts of the eye Dr J A van Heuven's paper, on "Retinal Detachment Following Inflammation," concerned the often overlooked role played by retinitis in the causation of detachment

The meeting adjourned from the hall of human anatomy to the adjoining scientific museum to witness the scientific demonstrations Mr Thomson Henderson explained the anatomic principles on which iridodialysis for glaucoma depends Mr J Cole-Marshall showed sketches of a hole in the macula as it appeared at different times Mr Lloyd Johnstone presented 4 patients of the same family with two types of hereditary cataract

It was then time for the congress to betake itself to Wadham College (whose buildings, dating from 1612, are little changed), there to have tea in "Ruskin's corner" of the gardens, at the invitation of the warden It is said that the gardens of Wadham, swept by branches of ancient cedars in a setting of holly and giant yews, owe their beauty to the perfect harmony that exists between them and the Jacobean architecture of the buildings This felicitous occasion will be remembered by many as long as they remember anything

In the evening the 145 members who had gathered at the congress, being more than had ever met at one time, came out in force to the annual dinner, held in the long and spacious Hall of Keble The college, built of variegated brick, is modern Its stated purpose is to provide a training for young men in "the principles of the Church of England" So it happened that England's churchmen, their course run, looked down from paintings exalted on the walls upon a goodly company of the living, who, having ceased from their labors for an interval, presented a scene of happiness and levity In the course of the dinner, Dr van Heuven, of Utrecht, Netherlands, rose and in a charming manner presented to the congress a beautiful and fittingly inscribed tile, baked in Dordrecht, as a token of gratitude from Netherland ophthalmologists for the assistance rendered them by their English colleagues during the late war

On Friday morning, the fifth, the program started with an address by Prof H Hartridge on "Recent Advances in the Physiology of Vision," which followed the substance of a paper published in the *British Medical Journal* (1:637 [April 27] 1946) However, no written language could have equalled words so fluently spoken and so graphically illustrated by free hand drawings, all of which made a difficult subject entertaining and instructive

This morning was the major one of the meeting, for, after a pause, there was to come the Doyne Memorial Lecture, which was delivered

by Prof A J Ballantyne. He chose for his subject "The State of the Retina in Diabetic Retinitis." He spoke first of the difficulty in defining diabetic retinopathy because of variations in the clinical picture that arise from time to time. These may represent either different stages in the development of the retinal changes or qualitative differences in the character of the diabetes, or they may be due to the influence of complicating factors. Drawing on a large series of diabetic cases of his own, he correlated their clinical and histologic phenomena and traced the relationship of both to the general disorder. Sketches of microscopic specimens and a set of drawings in colors of diabetic fundi, true to nature, gave evidence of the care with which this brilliant discourse was prepared.

The afternoon's session was opened with a paper by Mr Alex MacRae, entitled "Aspects of Thrombosis of the Central Vein." He cited cases from his practice in which a diagnosis of thrombosis was made and the patient recovered with good vision after prolonged rest in bed. He was convinced that in some of the instances of complete recovery the correctness of the original diagnosis should have been questioned. Mr John Marshall's paper, on "Sectional Recession and Treatment of Squint," and Mr O M Duthie's paper, on "Convergent Strabismus," each produced lively and prolonged argument, as does most experience with muscle operations whenever it is aired in meeting.

On Saturday morning, the sixth, the master summoned to the Hall a true friend of the congress, Mr Chesterton, who, since the first meeting, year by year has seen to it that the anatomic department is in readiness. The master presented to Mr Chesterton an envelope containing an expression of thanks and high regard. Mr Chesterton, in words that warmed everyone's heart, returned thanks to the congress and, to the regret of all, announced his approaching retirement from the department because of his age.

The annual general meeting was called. The council announced the names of the executive officers for the next year. As master, Mr F A Williamson-Noble, and as deputy master and honorary secretary-treasurer, Dr F A Anderson.

Dr J J Healey, in his paper entitled "Two Cases of Parinaud's Syndrome," took occasion to give a concise and critical review of the syndrome.

Prof Arnold Loewenstein is to be congratulated on his paper, entitled "Observations on the Blood Vessels of the Retina in Bulk." This represents a fine piece of original research, proving the development of capillaries within the walls of occluded retinal vessels, in an attempt to reestablish the circulation.

Dr C L Schepens, in his paper on "Goldmann's Hemispherical Projection Perimeter," brought out many points of practical use.

It remains to speak of the commercial exhibition, which, as in prewar days, filled the room assigned to it. It was an important and valuable part of the meeting, visited and revisited by all. The old firms from Oxford and Wigmore Streets in London were all represented. The delay in filling orders, the demand for instruments being great and urgent, lay, as in this country, in lack of materials and skilled workmen and in governmental restrictions.

In connection with this report of the first congress in six years not overshadowed by hostilities, it would seem opportune to outline the salient facts that had to do with the inception of an organization that today exerts so important and benevolent an influence. It truly represents the lengthening shadow of one man, Robert Walter Doyne. In 1886 Doyne founded the Oxford Eye Hospital. In 1900, a readership in ophthalmology was made possible in Oxford University through the munificence of Margaret Ogilvie, whose name it officially bears. Doyne received the appointment as the first reader, conjointly with which he became senior surgeon at Radcliffe Infirmary. This venerable charity was founded in 1770, the year before the New York Hospital received its royal charter from King George III. In the minds of Americans the Radcliffe is associated with the name of William Osler, whose memory is there kept fresh by the Osler pavilion.

In 1902, the university, having been convinced by Doyne of the important place that ophthalmology occupies in medicine, instituted a diploma in ophthalmology. This is a diploma conferred on candidates who have passed an examination held by the university after their completion of a course in a recognized school of ophthalmology, such as the one conducted by the Oxford Eye Hospital, the Royal London Ophthalmic Hospital (Moorfields) or the Royal Eye Hospital, in London. Of the twelve months instruction required, it is necessary that the last two be taken at Oxford.

The circumstance that directly led up to the establishment of the congress was a vacation course that Doyne gave for a number of years to ophthalmologists or any others interested in the specialty. The course lasted fourteen days, and at the end of this time lecturers and students were invited to remain for three days to discuss matters gone over and to see patients. Men not connected with giving the course were invited to come and read papers. The course became popular and drew men to Oxford from the Continent, the United States and the Dominions. In retrospect, the three days' conference was the present congress in embryo. It always sat at Keble, and custom, strong in England, exacts that the connection with Keble be continued.

In 1904 the British Medical Association met at Oxford, and, as it happily happened, the section of ophthalmology was housed at Keble and Doyne was appointed chairman. The meeting proved to be so successful scientifically and socially that Doyne, deeming the congress to be worthy of perpetuation, the next year sent out an invitation to members of the British Ophthalmological Society to come to Oxford, and so they and others from many countries, began to come in ever increasing numbers. In 1909, what had been known as the Oxford meeting was dignified with the name of the Oxford Ophthalmological Congress. In Great Britain, as elsewhere, most medical bodies bear a title that suggests that their membership is restricted to a certain locality. Thus, there are the British Ophthalmological Society, the North of England and the Midland Ophthalmological societies, the Irish Ophthalmological Society and the Club of Scottish Ophthalmologists, this last cognomen seemingly putting emphasis on a social, rather than a scientific, purpose. But there is but one congress, the Oxford Ophthalmological Congress, whose membership from all over the world bespeaks its universality. One of its founding members was

Wendell Reber, of Philadelphia, and among the original ten American members were Charles H. May, J. McReynolds, McCluney Radcliffe, Derrick T. Vail and Casey A. Wood. One day Harvey Cushing, on a visit to Oxford, attended unannounced to see for himself how eye men conduct their meetings. The congress is sometimes spoken of as the "Anglo-American Ophthalmological Congress."

The constitution of the congress states that it is for scientific and social intercourse of legally qualified medical practitioners who are interested in ophthalmology. The management is vested in a council, who elect the executive officers. There is no entrance fee or annual subscription, but a contribution is payable on each occasion that a member attends. The master wears the collar of his office, bearing his badge in colored enamel on gold, showing the calabar bean, the pilocarpus leaf and the fruit of *Atropa belladonna*.

Although the inauguration of the congress may be said to have been the coping-stone in Robert Walter Doyne's professional career, he wrought much more. As a practitioner he was a keen and accurate observer. He contributed no little to the literature of his time. His name is associated with such conditions as Doyne's family choroiditis, Doyne's iritis and Doyne's blepharoconjunctivitis.

In 1916, the year of Doyne's death, which occurred in the prime of his life, the council instituted the Doyne Memorial Lecture and caused a bronze medal to be cast for presentation to each lecturer. In looking over the names of the distinguished recipients, it appears that not all have been ophthalmologists. The allied specialties are represented, for it is the policy of the congress to be kept in touch with those branches of medicine on which ophthalmology is founded.

The fame of the Oxford Eye Hospital has grown side by side with that of the congress. It is an entirely independent unit, run by itself and proud of it. The hospital, with its forty-five beds, is housed in a building and on ground leased from the Radcliffe Infirmary—and this is the only connection between the two. Mr. P. H. Adams succeeded Doyne in charge of the hospital, and since 1941 Prof. Ida Mann has occupied the post. Her status in the university has been raised from that of a readership to that of a professorship.

Oxford was not damaged by "enemy action." Owing to this fact, Professor Mann was able to arrange an uninterrupted course that was designed to fill the needs of ophthalmologists in war and in peace. Among the Americans who came to attend the wartime congresses or to take Professor Mann's course, and who are so kindly remembered, were Colonel Derrick T. Vail and Majors Byron Smith, F. Phinizy Calhoun, Jr., Kenneth Fairfax and Joseph Kiug. In 1942 Viscount Nuffield became interested in the Oxford Eye Hospital and gave a donation for the equipment of a research laboratory there. This is housed in a temporary structure in the yard, and, as it is not endowed, in order that it may be fruitful, Oxford University is endeavoring to raise 250,000 pounds, of which 180,000 pounds are in hand.

When one stops to consider why the Oxford Ophthalmological Congress has endured and has increased in membership from 181, at its first meeting, in 1910, to 489 in 1939, certain characteristics of the meetings come to mind. The proceedings are leisurely conducted and are well balanced. The practical surgeon and the research worker may

be assured of hearing something that will be of particular interest. The attitude of those who participate in the discussions is frank and tolerant, which makes for good feeling and friendship. Finally, the seat of the congress is in the stately city of Oxford, which, with its traditions of seven hundred years of learning, has an allure all its own.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Brittain F. Payne, M.D., *Chairman*

Milton L. Berliner, M.D., *Secretary*

Regular Meeting, Oct. 21, 1946

INSTRUCTION HOUR

Controversial Points in Ocular Penicillin Therapy. DR. LUDWIG VON SALLMANN

The mechanism involved in the passage of penicillin across the blood-aqueous barrier and the means of influencing this passage were first discussed, and the following features of surface application were then considered: (1) continuance of penicillin activity in the conjunctival sac after instillation, (2) iontophoresis and (3) value of high drug levels in the aqueous.

The effects of intraocular injections of crystalline penicillin and of preparations of isolated species of *Penicillium* were described on the basis of histologic studies.

REPORT OF CASES

Malignant Teratoma of the Orbit: Six and One Half Years' Observation. DR. ALBERT V. SARADARIAN, Union City, N. J.

N. R., a female, was born at St. Francis Hospital, Jersey City, N. J., at full term, with low forceps delivery. A large tumor pushed the right eyeball markedly outward.

Exenteration of the right orbit was done, the eyelids being left intact. Five weeks later 4,878 millicurie hours of radium was given.

Pathologic study showed a malignant teratoma of the orbit. Photographs were shown of the condition at birth and at the time of the report.

DISCUSSION

DR. WENDELL L. HUGHES, Hempstead, N. Y.: I have had the opportunity of seeing this child several times during her lifetime, and I think Dr. Saradarian has managed the case excellently by keeping his hands off. I do not think that any operation would improve the local condition enough to make it cosmetically presentable. The only thing that could be hoped for is to get a prosthesis that would not be too disfiguring. Of course, to get life into such a prosthesis has not yet been done, but it is something on which I hope to be working in the near future. To make it possible to move the upper lid on the side of the prosthesis in unison with the lids of the other eye should not be too difficult a problem to solve.

Lipid Dystrophy of the Cornea DR SAMUEL FRANKEL and DR JULIUS SCHNEIDER

This process is characterized by a deep interstitial fatty and cellular infiltration of the cornea. The course is usually protracted and the condition painless and bilateral, though a long interval may precede involvement of the second eye. Berliner grouped several types of fatty metamorphosis of the cornea under the heading "lipid keratitis." The primary type is caused by a purely local disturbance, or is associated with a systemic disturbance, of lipid metabolism. The secondary forms consist in a degenerative change in long-standing disease of the cornea. The underlying pathologic process is the same in the two types. Heath divided the progress of these lesions into three stages: (1) the early, active phase, (2) the mature phase and (3) the retrograde phase.

CASE 1—M G B, aged 47, had a small foreign body removed from the right cornea in January 1944. About eighteen months later a residual scar began to grow and has continued to progress. Examination revealed a corneal opacity in the right eye, the central portion of which was solid, yellowish gray and vascularized and occupied the posterior half of the corneal stroma. The periphery was grayish white, consisted of numerous fine crystalline bodies and occupied the anterior third of the stroma.

CASE 2—M L F, aged 59, had a trephination on the right eye for glaucoma, after which a corneal opacity developed. The central portion of the opacity was yellowish, amorphous and vascularized. The periphery was less dense and was slightly flocculent in appearance.

Laboratory examinations, including determination of the cholesterol and the uric acid level of the blood, gave normal results in both cases.

DISCUSSION

DR ARNOLD KNAPP: Lipid disturbances of the cornea are important and extremely interesting, and it is timely that more of these cases are put on record. Am I correct in understanding Dr. Frankel to say that the blood cholesterol was normal in both cases? Has he been able to accomplish anything with treatment?

DR GERARD DE VOE: I want to ask about the use of corneal transplants in treatment of these conditions. Dr. Castroviejo has stated that in his experience transplantation is not indicated because the condition usually recurs in the transplant. I wonder whether any one else has had a similar experience.

DR SAMUEL FRANKEL: The blood cholesterol was within normal limits in both cases. Katz and Delaney, in discussing dystrophia adiposa corneae, and Heath, in his report on lipid interstitial keratitis, stated that studies of the blood cholesterol are inconclusive. In the majority of cases reported the blood cholesterol has been normal. In cases of lipid nephrosis, in which the blood cholesterol is high, corneal changes are usually absent. On the other hand, in cases of lipid dystrophy of the cornea, in which the blood cholesterol is normal, no estimation is made of perhaps more important fats which are present in the blood stream.

Treatment consists in attempting to trace and correct the underlying cause. Neither of our patients had any systemic disturbance of fat metabolism. No endocrine imbalance was found. Search for foci of infection gave negative results. The patients were placed on a diet low in fat and carbohydrate but showed no improvement. A corneal transplant was considered in case 1 but was not deemed advisable at that time because correctible vision in the affected eye was 20/40.

Wright (1936) reported a case of bilateral involvement in which keratoplasty was employed. The graft took successfully in one eye, whereas the other underwent fatty infiltration.

PAPER OF THE EVENING

Clinical Disturbances of the Oculomotor System DR. DAVID G. COGAN, Boston

Several oculomotor syndromes of clinical interest were presented and illustrated with moving pictures and lantern slides.

The first syndrome was internuclear ophthalmoplegia. It was pointed out that the manifestations were adequately explained by postulating a lesion in the medial longitudinal fasciculus, as illustrated by the 2 cases presented, there was a variation in the associated signs, depending on whether the lesion was situated anteriorly or posteriorly in the tract. In the cases presented the cause was multiple sclerosis.

The second syndrome, called "spasm of the near reflex," consisted in intermittent convergence, myopia and miosis. The etiologic factor in the cases presented was hysteria, and 2 of the patients were "cured" by lenses of negative dioptric power.

In the third syndrome, called "oculomotor short circuits," some of the ocular muscles are presumed to become innervated by nerves other than those originally intended. The cases illustrating this condition were those of (1) aberrant regeneration of the third nerve, (2) the jaw-winking reflex and (3) an unnamed anomaly, in which there were a rhythmic upward and downward movement of one eye and a simultaneous extorsion and intorsion of the other eye.

The fourth, and final, syndrome was that of pseudo-ophthalmoplegia in infants, with a characteristic paralysis of voluntary lateral gaze but with preservation of haphazard gaze. The conspicuous feature in the 2 cases illustrating this syndrome was a peculiar jerk of the head, by which the infant attempted to compensate for the oculomotor disturbance. Noteworthy, also, was the absence of the fast phase of labyrinthine nystagmus.

DISCUSSION

DR. HAROLD W. BROWN. In a relatively few minutes, Dr. Cogan has shown through moving pictures and slides, classic cases of these various syndromes, which must have taken him years to collect and classify. The first slide, showing the neuroanatomy of the oculomotor nerves and their connections with the conjugate centers of lateral gaze, of convergence and of accommodation through the medial longitudinal fasciculus, has enabled us to follow the neurologic explanation of these interesting syndromes and will surely help us to recognize cases of these disturbances when we encounter them.

Marshall and Laund (*AM J OPHTH* 19:1085 [Dec] 1936) reported 100 cases of multiple sclerosis. In their series, about 10 per cent of the patients had oculomotor disturbances, about 6 per cent had paresis of individual muscles, and 4 per cent had paresis of conjugate movements. The authors cited extensively from the cases in the literature, in the majority of which paresis or paralysis of individual muscles was present. In about 30 or 40 per cent of the cases in one series there was a history of transient diplopia. This would fit in well with Dr Cogan's explanation of these transient pareses, either of conjugate movements or of individual muscles. I have had several cases in which oculomotor dysfunction was associated with multiple sclerosis, in 1 case in particular there was a paresis of divergence. I should like to have Dr Cogan tell us something about the divergence center—whether or not it exists—and, if so, its approximate location and whether, in his experience, multiple sclerosis is a common cause of divergence paralysis.

The condition that Dr Cogan calls spasm of convergence, or the convergence reflex, is always thought of in terms of accommodation. The few cases of the disturbance that I have seen were in young girls and were always associated with neurosis or hysteria.

Dr Cogan states that aberrant regeneration of the third nerve, in which there was paralysis of both elevator muscles of the eye, was usually due to birth injuries. In the cases which I have had, with paresis or paralysis of both elevator muscles, with or without ptosis, there was usually a history of prolonged labor, and at times scars or forceps marks were present on the head. I have followed several of these patients, whose paresis seems to improve as they get older. First, there is complete ptosis, and the eye cannot be raised to the horizontal position, as time goes on, both the levator of the lid and the elevator muscles of the eye function well enough to open the eye partially and raise the eyeball above the horizontal position.

I should like to ask Dr Cogan whether he has observed any improvement in a paralyzed muscle in the cases he has classified under aberrant regeneration of the third nerve.

DR HENRI BIRNBAUM. I should like to ask how the patients with spasm of convergence act after instillation of atropine.

DR D M ROLETT. I should like to ask whether a caloric test was done in the last case. It seemed to me that the rotatory movement had the value of the Bárány test, and I wonder whether the disturbance in this case was not associated with nystagmus.

DR DAVID G COGAN. First, in regard to Dr Brown's point about divergence paralysis. As you know, the problem of the localization of a divergence center is a hardy perennial. Fortunately or not, depending on the point of view, there is rarely an opportunity for autopsy on patients who have a sufficiently discrete lesion to mean anything. I know of only 3 cases with autopsy in which divergence paralysis was one of the clinical manifestations. In 1 case there was a hemangioma in the midbrain, and in the others lesions of the cerebellum were present which may well have pressed on the floor of the fourth ventricle. It is hard to fit that localization in with the many conditions which cause divergence paralysis. I had the interesting experience of finding a typical divergence

paralysis in a patient with polyneuritis, with no evidence of intracranial disease other than the paralysis. I had another interesting case in which there was a divergence paralysis with Wernicke's disease. Subsequently this patient had a convergence paralysis, suggesting a relationship between the divergence and the convergence center. As to the localization of the center, I have nothing to offer that is illuminating. I do not recall having seen divergence paralysis associated with multiple sclerosis.

As to improvement of the ocular movements following aberrant regeneration of the third nerve, the history in most of the cases presented this evening indicated that the anomaly was congenital, there having been a ptosis at birth, with spontaneous elevation of the eye beginning in three to five months. But when the patient was seen at the age of 5 years or older, the condition was stationary.

As for treatment of spasm of the near reflex, atropine "cures" it, just as do minus glasses, another effective means of treatment is prisms, base out. The use of minus glasses seemed to be the most compatible with school work.

As for the presence of congenital nystagmus in babies with pseudo-ophthalmoplegia, these patients had no nystagmus. Rotating the patients as I did was analogous to a Bárány test, this resulted in a maintained deviation of the eyes to one side, there being a characteristic absence of the fast phase of labyrinthine nystagmus.

Book Reviews

Ophthalmology in the War Years Edited by Meyer Wiener, MD
Volume I (1940-1943) Price, \$13 50 Pp 1166 Chicago The
Year Book Publishers, Inc, 1946

The idea of a review of the literature on ophthalmology during the war years was suggested to the Subcommittee on Ophthalmology of the National Research Council, who were fortunate enough to get Dr Meyer Wiener to act as editor in chief. As Dr Wiener says in the preface, the task of securing associate editors under present conditions was particularly difficult, as can be easily understood. Yet the subdivision of the work and the excellent selection of co-editors reflects great credit on Dr Wiener. The book brings a bibliography and an abstract of the important articles, as well as a general review, of each subject which appeared in the literature from the years 1940 to 1943. Unfortunately, the literature from Great Britain and from the Continent could not be included in this volume, but the literature from Latin America was available, thanks to the excellent cooperation of Dr Moacyr Alvaro and his associates. The table of contents lists the following subjects and the respective authors:

"Anatomy and Embryology," John J Prendergast, "Aqueous Humor," Jonas S Friedenwald, "Biochemistry, Pharmacology and Toxicology," David G Cogan and W Morton Grant, "Color Blindness," Louise L Sloan, "Comparative Ophthalmology," Helenor Campbell Wilder, "Congenital Anomalies," Arthur M Yudkin, "Conjunctiva," John G Bellows, "Cornea and Sclera," Ramon Castroviejo, "Electrophysiology," S Howard Bartley, "Experimental Pathology," Peter C Kronfeld, "General Pathology and Bacteriology," Georgiana Dvorak-Theobald, "Glaucoma," Otto Barkan, "Hygiene, Sociology, Education and History," Windsor S Davies, "Industrial Ophthalmology," Hedwig S Kuhn, "Injuries," Robert J Masters, "Instruments and Apparatus," H Rommel Hildreth, "The Lens," Ray E Daily and Louis Daily Jr, "Lids and Lacrimal Apparatus," Harold F Whalman, "Methods of Examination," Leo L Mayer, "Neuro-Ophthalmology," P J Lemfelder, "Ocular Muscles," George P Guibor, "Orbit, Eyeball and Sinuses," William L Benedict, "Physiologic Optics," Hermann M Burian and Kenneth N Ogle, "The Pupil," Henry Minsky, "Refraction and Accommodation," E Merle Taylor, "Retina and Vitreous," Hugo Lucio, "Surgery of the Eye," Bennett Y Alvis, "Systemic Diseases Syphilis, Parasites," Joseph Igersheimer, "Therapeutics," Frederick C Cordes and Samuel D Aiken, "Trachoma," Phillips Thygeson, "Tumors," Algernon B Reese, "Uveal Tract," William M James

It is at once apparent that the subject has been admirably subdivided and that Dr Wiener was fortunate enough to obtain an expert to review each part. The many references that are given in the bibliography are astonishing, and it is clear what a laborious undertaking their examination must have entailed. The critical reviews in each

chapter are particularly excellent and useful. The second volume will include the literature beginning January 1944, and ending in June 1946.

The book making is excellent, with good paper and distinct type. The author and his co-editors are to be congratulated on the successful outcome of this volume. The second volume, on its appearance in 1947, will complete a most useful and excellent summary of ophthalmologic literature of a part of the world during the war years.

ARNOLD KNAPP

Die Erkrankungen des Augenhintergrundes (Diseases of the Fundus)

By Professor Adalbert Fuchs. Pp 287, with 66 illustrations in colors on 44 plates. Vienna. Franz Deuticke, 1943.

From lectures, and with the addition of a number of pictures of unusual, yet characteristic, cases of diseases of the fundus, the author has compiled this book to serve as an aid to physicians and oculists, without attempting to write a formal handbook with many literary references. The typical diseases as they relate to internal medicine, neurology, dermatology, surgery and pediatrics are briefly but clearly described, with particular attention to the fundus pictures and the subjective symptoms, and a complete index is added. The author emphasizes that, in addition to the fundus picture, knowledge of the anatomy of the lesion is of the greatest aid in the diagnosis of a disease of the fundus. He has therefore added many histologic sections which are easily recognized by the specialist without going into minute histologic details, and which serve their purpose best in the form of drawings, rather than of photographs.

The book is divided into chapters dealing with the following subjects: varieties of the normal fundus, congenital anomalies, diseases of the optic nerve, glaucoma, tuberculosis of the posterior eyeball, syphilis of the posterior eyeball, myopia, tumors, retinal detachments and injuries.

The author has succeeded in covering an important and most interesting part of the diseases of the eye in a book which serves admirably as an addition to the usual textbook. The plan to illustrate the ophthalmoscopic appearance of each lesion with the associated histologic picture is unique and will be found most useful and instructive by every student of ophthalmology. The print and paper are excellent, and the drawings and histologic pictures of the fundus, in color on forty-four plates, reflect great credit on the artist, Hugo Keilitz.

ARNOLD KNAPP

Lehrbuch der Augenheilkunde. Seventeenth edition. Edited and enlarged by Dr Adalbert Fuchs. Pp 916, with 362 illustrations and 5 colored plates. Vienna. Franz Deuticke, 1943.

Dr Adalbert Fuchs took over the editorship of Ernst Fuchs's well known textbook and a new edition appeared in 1939. Notwithstanding the change that had taken place in the character of diseases of the eye in recent decades, especially in the severe forms of corneal ulceration and conjunctivitis, the description of the external diseases was not curtailed. On the other hand, Fuchs recognized the advances that have taken place in knowledge of diseases of the fundus and their relations to general medicine, so that this part of the book was enlarged. The chapters on tumors,

neurology and muscles were also added to. Inherited ocular disorders received more attention, as evidence of the large number of congenitally blind to be found in the homes for the blind. Treatment of ocular diseases was more fully described. Realizing the importance of pathology in the understanding of diseases of the eye, the author added more colored illustrations, which were taken from his excellent "Atlas of the Histopathology of the Eye."

This revised edition was so well received that a new, seventeenth, edition appeared in 1943, notwithstanding the difficulties of the war years. A number of new illustrations have been added in this new edition, and among the new features the important treatment with sulfonamide drugs must be mentioned. A desirable and useful addition is a chapter describing unusual syndromes in which general conditions are associated with ocular symptoms. These are frequently spoken of in the medical literature of today, and their descriptions are often not easily found in the usual medical textbooks.

The paper and printing are excellent

ARNOLD KNAPP

Journal of Gerontology Volume 1 Number 1 Published quarterly for the Gerontological Society, Inc. Part 1 Annual subscription, \$6, pp 152. Part 2 Non-Technical Supplement (separately), \$3, pp 84. Springfield, Ill. Charles C Thomas, Publisher, 1946

This new arrival in periodicals, dealing with the various aspects of aging, physiologic and pathologic, their social and medical implications, purposes "to add life" to years, not just years to life—surely a laudable aim, if not just a *primum desiderium*.

Part 1 presents a number of interesting, if somewhat disconnected, chapters, entitled, "Gerontology," by Lawrence K. Frank, "Logarithmic Increase in Mortality as Manifestation of Aging," by Henry S. Simms, "Relation Between Age of Stem Tissue and Capacity to Form Roots," by P. W. Zimmerman and A. B. Hitchcock, "Aging in Nutritionally Deficient Persons" by Tom D. Spies and Harvey S. Collins, "Prolongation of Life with Prevention of Leukemia by Thymectomy in Mice," by Jacob Furth, "The Hodson Community Center," by Dora Fuchs and Harry Levine, "Budgeting for Social Security," by W. R. Williamson, "Attitudes Toward Aging and the Aged Primitive Societies," by Leo W. Simmons, "Involution of Tissues in Fetal Life," Arthur T. Hertig, and, finally, "Shakespeare's Attitude Toward Old Age," by John W. Draper. To each of these chapters is appended an abstract in English, French, Spanish and Russian, a rather significant indication of the trend of the times.

The non-technical supplement (part 2) abstracts these articles practically unchanged, however, it presents in addition, under the heading of "Current Comment," a number of lighter items, such as "The Fountain of Youth," "The Debt of the Survivors," "Surgery for the Aged," "Shaw and Beveridge," "Fun at Sixty," *et tuhi quanti*.

There are book reviews, too, a list of books received, an index of current periodical literature (on gerontology) and a glossary. Varied fare, indeed, which may interest those who, as Draper notes, like to browse through the ages, meaning in medical by-ways, and may appeal to ophthalmologists here and there, even if they are not concerned with the practical implications of gerontology.

PERCY FRIDENBERG

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ASSOCIATED SYSTEMIC FACTORS IN RETINITIS PIGMENTOSA

ISADORE GIVNER, M D
AND
MAURICE BRUGER, M D
NEW YORK

THIS study was prompted by 2 cases of retinitis pigmentosa with unusual associated conditions. An attempt to determine whether these additional factors were constantly present led to laboratory investigations, of which this paper is a preliminary report. The present series includes 14 patients and hence is not large enough to justify one in drawing absolute conclusions.

CASE 1—R P, a woman aged 43, had had poor vision for many years, was overweight and had disturbed menstruation and loss of the superotemporal field of both eyes. A diagnosis of tumor of the pituitary gland was made elsewhere, and the patient was referred to Dr Israel Wechsler for neurologic study. His examination, which included roentgenographic study of the sella turcica and encephalographic tests (these showed normal ventricles and cisterns), revealed nothing abnormal. We interpreted the fields as due to breaking through of an annular scotoma, quite in keeping with the retinitis pigmentosa, which was well developed. The unusual feature of the case was a spinal fluid pressure of 300 mm of water.

Could this increased cerebrospinal fluid pressure occur as an associated condition with retinitis pigmentosa, just as the association of the latter with epilepsy, acrocyanosis and Raynaud's disease has previously been described? What are the spinal fluid pressure and chemistry in retinitis pigmentosa? A review of the literature failed to disclose any reference to these factors.

CASE 2—A man aged 34 had had difficulty with seeing most of his life. Ten years previously he noted the onset of deafness and asthenia. His fatigue had so increased that he had to rest six days out of seven. His mother and father were first cousins. The findings on ophthalmologic examination were typical of retinitis pigmentosa, with tubular fields, posterior cortical opacities, waxy disks, threadlike arteries, bone corpuscle-shaped pigment throughout the fundus and night blindness. Vision was 10/200 in the right eye and 20/200 in the left eye with correction. His spinal fluid was under normal pressure, but the total protein measured 194 mg per hundred cubic centimeters (normal 15 to 40 mg) and the chlorides 1,195 mg per hundred cubic centimeters (normal 700 to 750 mg). No cells were present. The albuminocytologic dissociation was similar to that found with

Read before the New York Society for Clinical Ophthalmology, March 4, 1946.

From the Ophthalmological and Medical Services, New York Post-Graduate Medical School and Hospital.

the Guillain-Barre syndrome. In addition, his basal metabolic rate was 17 per cent below the average normal, moreover, creatinuria was present.

Males do not normally excrete creatine, as it is converted into creatinine before excretion. Tierney and Peters,¹ studying 22 normal male subjects, found no creatine in the urine. Steinach, Kun and Peczenik² stated that androgen deficiency exists if the amount of creatine in the urine is 10 per cent or more of the combined values of creatine and creatinine. Are these findings peculiar to this case, or are they the rule in cases of retinitis pigmentosa?

Wibaut³ stated that there are two types of retinitis pigmentosa. In cases in which the disease is a dominant characteristic, it is practically never associated with nerve lesions. The recessive type is associated with deafness and other evidences of involvement of the central nervous system.

A review of the literature on retinitis pigmentosa leads to the conclusion that the disease is due to dysfunction of the autonomic and endocrine systems, hereditary in nature and manifest in the germinal anlage. We feel that factors which influence the rate of development of this disease might be revealed by detailed physical and laboratory studies. It is hoped that when these associated disturbances are corrected the blindness which is the usual outcome of this disorder may be delayed.

With this in mind, the patients investigated were admitted for hospital care for four days, during which studies of various factors were undertaken.

1 Basal metabolism. Wolff⁴ reported that subnormal temperatures are associated with retinitis pigmentosa, she suggested that this finding is a manifestation of a reduced "dynamic effect" and regretted that she did not have facilities for carrying out basal metabolic studies in order to prove her point.

2 Spinal fluid pressure and chemistry.

3 Vitamin content of the blood plasma. Vitamin A deficiency as a cause of night blindness is well known. The adrenal cortex has a large storage of vitamin C and depends on this for its proper function. Giroud, Santa, Martinet and Bellon⁵ maintained that a rise in the ascorbic content of the adrenal cortex induces a corresponding increased secretion of cortical hormones and that an optimum level of vitamin C

1 Tierney, N. A., and Peters, J. P. *J. Clin. Investigation* **22** 595, 1943.

2 Steinach, E., Kun, H., and Peczenik, D. *Wien klin. Wchnschr.* **49** 388, 1936.

3 Wibaut, F. *Klin. Monatsbl. f. Augenh.* **87** 298, 1931.

4 Wolff, L. L. *Am. J. Ophth.* **23** 275, 1940.

5 Giroud, A., Santa, N., Martinet, M., and Bellon, M. T. *Bull. Soc. chim. biol.* **23** 108, 1941.

is required for the proper functioning of the cortical cells. The relationship of the adrenals to other ductless glands, especially the anterior lobe of the pituitary, the pancreas and the thyroid, is well recognized

4 Hepatic function Takahashi⁶ found 12 cases of retinitis pigmentosa among many cases of diseases of the liver. He concluded that damage to the liver was a factor in the pigmentary disturbance. In line with this work was that of Kalt,⁷ who in 1937 produced pigmentary changes in the retina of rabbits by the subcutaneous injection of 1 cc of 4 per cent sodium iodate per kilogram of body weight every other day. Within ten days a scattering of pigment was visible in the retina. Histologically, there were many clumplike aggregations of pigment, with partial destruction of the rods and cones. All animals had cirrhotic changes in the liver. He therefore concluded that patients with retinitis pigmentosa may have a hepatic disturbance. The cephalin-cholesterol flocculation procedure of Hanger, which is a sensitive test for hepatic damage, was used in our study.

5 Serum cholesterol The literature reveals that hypercholesteremia has been frequently observed in patients with retinitis pigmentosa. Wolff attributed great significance to this finding, since she reported values of 360 to 380 mg per hundred cubic centimeters of blood in cases of well advanced retinitis pigmentosa.

6 Creatinine and creatine in the urine Schrire⁸ found an increased urinary excretion of creatine in cases of acromegaly and used this test to distinguish chromophilic from chromophobic tumors of the pituitary before operation. He concluded that some hormonal factor of the pituitary gland is involved in the control of creatine metabolism.

7 Pupillographic evidence Lowenstein and Friedman⁹ stated that tonohaptic reactions (a term denoting a long latency period for contraction, a more or less good contraction to light and a long latency period for redilation) were found in animal experiments with lesions either in the diencephalon or in its connections with the mesencephalon.

McDonald and Adler¹⁰ stated that studies carried out on patients with retinitis pigmentosa suggest, but do not conclusively prove, pituitary dysfunction. Tests previously carried out by others to support the theory

6 Takahashi, T. *Arch f Ophth* **116** 143, 1925

7 Kalt, E. *Bull Soc d'opht de Paris* **49**:304, 1937

8 Schrire, I. *Quart J Méd* **6** 17, 1937

9 Lowenstein, O., and Friedman, E. D. *Pupillographic Studies. Present State of Pupillography, Its Method and Diagnostic Significance*, *Arch Ophth* **27** 969 (May) 1942

10 McDonald, P. R., and Adler, F. *Pigmentary Degeneration of Retina. Role of Melanophore Hormone of Pituitary Gland in Pigmentary Degeneration of Retina*, *Arch Ophth* **27** 264 (Feb) 1942

of pituitary dysfunction in patients with retinitis pigmentosa have demonstrated thyrotropic substance in the urine, abnormalities of water and salt metabolism, diminished dextrose tolerance and the presence of a melanophore-dispersing substance in the blood and urine Zondek,¹¹ Viallefont¹² and Mamola and Bellina¹³ have reported on the administration of preparations of the pituitary gland in cases of this disorder Their reports, though not enthusiastic, have all claimed definite subjective improvement

Certain embryonic and clinical relationships further suggest the association of retinitis pigmentosa with pituitary dysfunction Moehlig and Pino¹⁴ found a high-arched palate in each of 21 cases of retinitis pigmentosa Disturbances in the embryonic development of the hard palate is responsible for the high arching It is generally accepted that the pituitary gland develops from the ectoderm in the roof of the mouth and the neural ectoderm in the floor of the third ventricle Ingram¹⁵ recently reviewed the nerve fiber connections between the pituitary gland and the hypothalamus The latter regulates endocrine functions and their interrelations, as well as autonomic functions

Pines, Collin¹⁶ and Greving and Stengel stated that two sets of nerve bundles pass from the diencephalon to the pituitary gland, one of them arises from the nucleus supraopticus and can be traced to the tuber cinereum, the second bundle arises directly from the nucleus paraventricularis, at the third ventricle These fibers might influence the hormone production of the gland

The close embryonic and anatomic association of the pituitary gland, the hypothalamus and the eye also suggest a close physiologic connection Zondek stated that retinitis pigmentosa may be the sole clinical evidence of diencephalic disturbance Syndromes like the Laurence-Moon-Biedl syndrome lend support to this contention, as does the association of retinitis pigmentosa with Hirschsprung's disease (congenital megacolon) and cachexia hypophyseopriva Zondek¹⁷ described 4 cases of retinitis pigmentosa in which marked disorders of the diencephalic function could be shown

11 Zondek, H Disease of the Endocrine Glands, Baltimore, William Wood & Company, 1935

12 Viallefont, H Ann d'ocul **173** 33, 1936

13 Mamola, P, and Bellina, G Rassegna ital d'ottal **4** 699, 1935

14 Moehlig, R C, and Pino, R H Retinitis Pigmentosa Etiologic and Clinical Implications Based on Twenty-One Cases, Arch Ophth **23** 1257 (June) 1940

15 Ingram, W R Psychosom Med **1** 48, 1939

16 Collin, R Compt rend Soc de biol **118** 1560, 1935

17 Zondek, S G, and Kohler, cited by Levy-Wolff, L Am J Ophth **23** 275, 1940, Klin Wchnschr **4** 809, 1925, Deutsche med Wchnschr **47** 1520, 1921

Laboratory Data on Fourteen Patients with Retinitis Pigmentosa †

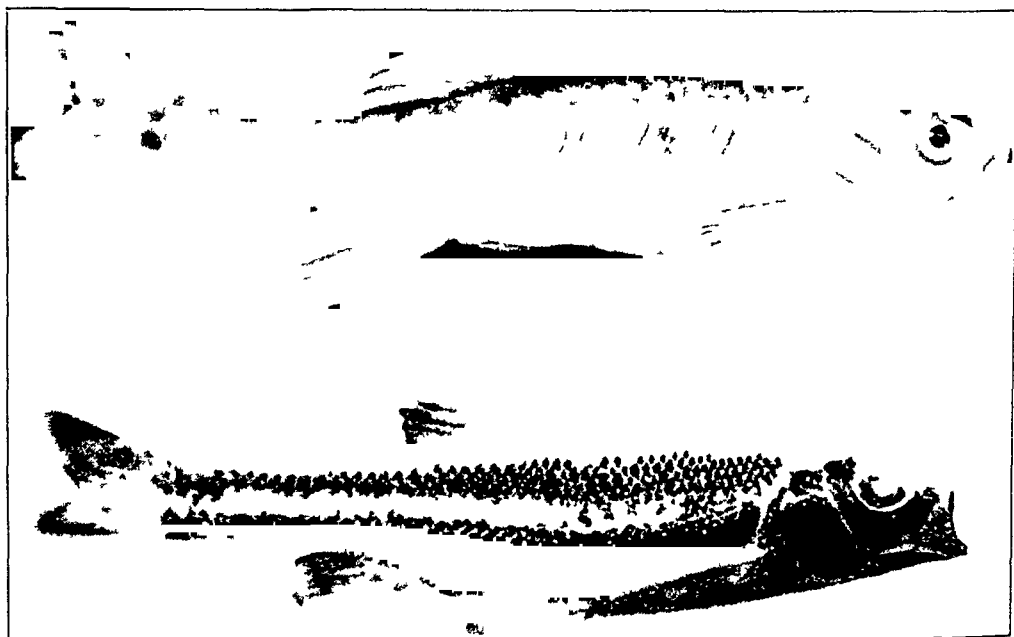
Case	Age	Sex	Cerebrospinal Fluid		Basal Metabolic Rate, % Normal	Urinary Creatinine, Mg / 24 Hr	Hepatic Function		Serum Vitamin			Pupillography †	
			Pressure, Mm H ₂ O	Total Protein, Mg / 100 Cc			Cephalin Cholesterol Flocculation	Sulfo-bromo-phthalen Retention	Serum Cholesterol, Mg / 100 Cc	Vitamin A, Blue Units / 100 Cc	Total Carotenoids, Units / 100 Cc		Plasma Vitamin C, Mg / 100 Cc
1	34	M	80	194	-17	150	-	-	240				C S L
2	43	F	300	215	-21	340	+	+	245				C S and C P
3	26	M			-9	1,200	+	+	195				Tonohaptic reaction
4	23	M	140	271	-16	300	+	+	150			0.9	Tonohaptic, cap micro neg
5	25	M	144	39.6	-5	500	+	+	250			0.2	C S L
6	17	M	110	50	-6	123	-	-				0.75	Tonohaptic reaction
7	46	M	140	41.9	-15		-	-	265	20		0.3	Tonohaptic reaction
8	39	F	160	55.5	-5	260	-	-	185	10	100	0.1	Epilepsy, tonohaptic reaction
9	43	M	188	39.9	+1	516	-	-	185	15	84		Tonohaptic reaction
10	30	M	120	40.2	-1		-	-	180	20	340	0.65	
11	22	M	110	32.2		488	-	-	185	10	102	0.05	Deaf mute
12	25	F	120	24.2	+8	470	+	-		15	87	0.45	Cap micro neg
13	42	M	70	24.3	+3	1,040	-	-	230	15	144	0.25	Tonohaptic, deaf mute
14	53	M					-	-					Tonohaptic reaction

* The corresponding normal findings are as follows: spinal fluid pressure, 100 to 150 mm of water, total proteins, 15 to 40 mg per hundred cubic centimeters, basal metabolic rate, -10 to +10 per cent of the average normal, cephalin cholesterol flocculation test, - to +, sulfobromophthalen retention test, less than 10 per cent retention in one hour after injection of 5 mg per kilogram of body weight, creatinine in the urine, none in males, serum cholesterol, 160 to 230 mg per hundred cubic centimeters, total serum carotenoids, 50 to 100 units per hundred cubic centimeters, vitamin A, 10 to 20 blue units per hundred cubic centimeters, ascorbic acid in the blood plasma, 0.7 to 1.4 mg per hundred cubic centimeters

† O S L indicates a lesion of the central sympathetic nervous system, and C S and C P, involvement of the central sympathetic and parasympathetic nervous system, tonohaptic reaction implies a lesion either in the diencephalon or in its connections with the mesencephalon, and cap micro neg indicates no change in the capillaries of the nail bed as seen in microscopic examination

Although the work of McDonald and Adler speaks against any role of the melanophore-stimulating hormone in pigmentary degeneration of the retina, sufficient evidence is at hand to support the contention that the pars intermedia of the posterior lobe contains a melanophoric stimulant (figure). Interesting is the fact that dispersion of melanosomes has been caused by aqueous humor, as reported by Van Dyke.¹⁸ This suggested to Moehlig and Pino that secretion of the pars intermedia may be contained in the eye.

8 Audiometric observations. Wolff showed that the inner ear, the retina and the choroid are supplied by the same set of vasomotor fibers, and she expressed the belief that this may be responsible for the hearing defect commonly observed in patients with retinitis pigmentosa. In



Erythrophore reaction in a minnow (*Phoxinus laevis*), demonstrating the presence of a chromatophore-stimulating hormone, as suggested by Zondek and Krohn. The upper figure shows the normal minnow, the lower figure, the characteristic red colorization appearing one-half hour after injection of posterior pituitary solution (intermedin).

some series, reported loss of hearing has been noted in as many as 10 per cent of these patients.

9 Capillary microscopy. Brown and Whitney¹⁹ found what they considered unmistakable evidence of a generalized peripheral vascular disturbance of the capillary type.

18 Van Dyke, H. B. *The Physiology and Pharmacology of the Pituitary Body*, Chicago, University of Chicago Press, 1936.

19 Brown, W. M., and Whitney, E. L. Peripheral Vascular Picture in Retinitis Pigmentosa, *Arch Ophth* 24 984 (Nov) 1940.

SUMMARY AND RESULTS

1 No abnormalities in pulse rate, blood pressure or temperature were observed in 14 patients with retinitis pigmentosa

2 The serum cholesterol was within normal limits in 7 of 11 patients on whom this determination was made. In 3 patients it was only slightly elevated

3 The basal metabolic rate was within normal limits for 8 of 12 patients. For 4 patients the rate varied from 15 to 21 per cent below the average normal

4 Eleven patients had creatinuria. This series included 8 males and 3 females

5 The spinal fluid pressure was increased in 3 of 12 patients, but readings in most of the other patients bordered on the upper limit of normal, rather than falling at the lower levels. In 3 of 12 patients the total protein content of the spinal fluid was definitely increased. In the remainder, normal values were observed

6 Hepatic damage was not demonstrable in any of the 12 patients investigated

7 The fasting ascorbic acid content of the plasma was reduced in 7 of 9 patients on whom this determination was carried out. The 2 patients with normal values had been taking ascorbic acid before the test was carried out. Vitamin A studies on the serum of 7 patients gave normal values

8 In 11 patients, pupillographic studies showed tonohaptic reactions and other evidences of diencephalic disorders

9 Analysis of the blood for retention of urea nitrogen and determination of the specific gravity of the urine after administration of pitressin failed to reveal any measurable impairment in renal function in 13 patients

10 Physical examination, including neurologic studies, gave essentially normal findings except for the high incidence of high-arched palate and nerve deafness, as revealed by audiometric tests. Seven of 8 patients thus studied revealed impairment of hearing. Two patients were deaf-mutes

11 In 2 patients microscopic examination failed to reveal any abnormalities in the capillaries of the finger bed

Dr Conrad Berens and Dr Willis Knighton gave us permission to examine 4 patients of the present series from their clinics at the New York Eye and Ear Infirmary

USE OF FROZEN-DRIED CORNEA AS TRANSPLANT MATERIAL

IRVING H LEOPOLD, M D
AND
FRANCIS HEED ADLER, M D
PHILADELPHIA

KERATOPLASTY has reached the stage today at which the demand for donor corneas has exceeded the supply. The small supply is largely due to the difficulty in preserving all available corneal tissue until the time at which it is needed. With the present methods of preservation, corneal tissue held over seventy-two hours is believed to be unsatisfactory for transplantation. Such tissue is usually kept in Ringer's solution or isotonic solution of sodium chloride or in a moist chamber at a temperature of 2 or 3 C¹. In an effort to increase the donor supply, the present experiment was undertaken. The purpose of the experiment was to determine the value of frozen-dried cornea (Weiss method)² for corneal transplantation, as suggested by the preliminary experiments with rat cornea of Weiss and Taylor³.

METHOD

Transplants of frozen-dried rabbit cornea, prepared by Dr Paul Weiss, were attempted on 75 normal rabbit eyes. The technics employed were as follows:

A Anesthesia

- 1 Local anesthesia
- 2 Open drop ether anesthesia
- 3 Intravenous injection of Dial or pentobarbital. This method proved superior to the use of ether because of less interference with the operative field.

From the Department of Ophthalmology of the University of Pennsylvania.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Pennsylvania.

1 Castroviejo, R. Keratoplasty. Comments on Technique of Corneal Transplantations, Source and Preservation of Donor Material, *Am J Ophth* **24** 1 and 139, 1941.

2 Weiss, P, and Taylor, A. C. Repair of Peripheral Nerves by Grafts of Frozen-Dried Nerve, *Proc Soc Exper Biol & Med* **52** 326, 1943. Taylor, A. C. The Rates of Freezing, Drying and Rehydration of Nerves, *J Cell & Comp Physiol* **25** 161, 1945.

3 Weiss, P, and Taylor, A. C. Transplantation of Frozen-Dried Cornea in the Rat, *Anat Rec* **88** 464, 1944.

B Preoperative preparation

- 1 Five drops of penicillin solution, 500 Oxford units per cubic centimeter of isotonic solution of sodium chloride, was given thirty minutes prior to operation
- 2 Two drops of a 10 per cent emulsion of neo-synephrine hydrochloride ten minutes before operation
- 3 Two drops of atropine 2 per cent sulfate were instilled ten minutes prior to operation
- 4 Lashes were cut routinely, but the surrounding skin was not shaved routinely
- 5 Sterile drapes were used in all but the initial operations

C Corneal sectioning

- 1 The double-bladed knife of Castroviejo or the corneal trephine was used. The trephine was 4.5 mm in diameter, and similar to the one devised by Townley Paton. The size of the segment cut with the double-bladed knife varied, but not one was cut smaller than a 4 mm square.
- 2 No particular attempt was made at beveling. The trephine donor segments were cut with the same trephine as was used to cut the recipient cornea.
- 3 The donor segments were always prepared before excising the recipient cornea.
- 4 The donor cornea was transplanted to the corneal bed on a moistened iris repositor. No forceps were used in handling the graft.

D Corneal sutures

- 1 Because of the high fibrin content of rabbit secondary aqueous, the grafts will adhere to the recipient bed without sutures. However, one edge frequently rode up as the anterior chamber formed, so sutures were used in the majority. The Castroviejo suture¹ was employed. The suture material was 000000 black surgical silk on atraumatic curved needles.

E Solutions used during operation

- 1 The fibrin in the secondary aqueous humor is so great that it often forms a coagulated mass in the recipient bed before the transplant is put in place. This interferes with a proper fit. Therefore the recipient bed was irrigated either with a 3 per cent solution of sodium citrate or with heparin before fitting the transplant.
- 2 At the close of each operation 5 drops of penicillin solution, 500 Oxford units per cubic centimeter, and 1 drop of a 2 per cent solution atropine sulfate were instilled. Suturing of the lids, although providing better support to the transplant, resulted in greater frequency of infection in spite of the instillation of penicillin and was therefore abandoned.

F Dressings

Eyes were examined daily for the first three days, and penicillin and atropine solutions instilled once a day. Sutures were removed under local anesthesia induced with 0.5 per cent tetracaine hydrochloride on the third day. The longer the suture remained, the more frequently did corneal vascularization occur. Thereafter, eyes were examined every other day for two weeks and then weekly. This technic was derived

from the recorded experience of Castroviejo,¹ Thomas,⁴ Filatov⁵ and Cuthbert⁶ and through our own trials and errors

G Material for transplantation

- 1 The initial specimens of frozen-dried tissue consisted of rabbit cornea, not including the limbus, cut in half before dehydrating and freezing. This necessitated cutting the tissue for transplantation after rehydration. This tissue was cut by first marking the area to be sectioned with the double-bladed knife or trephine while the tissue lay in the rehydrating fluid. The surrounding tissue was grasped with forceps and the section completed with scissors. Care was exercised to avoid handling, with the forceps, the particular part to be transplanted.
- 2 The second series of specimens consisted of sections of rabbit cornea cut into 4 to 5 mm squares prior to freezing and dehydration. Tissues prepared in this manner were rehydrated and the best-shaped ones selected, the others discarded. The recipient bed was cut to fit the transplant.
- 3 The third series of specimens consisted of entire corneas with a 2 to 3 mm rim of scleral tissue. A plastic mold was made on which these specimens were placed, prior to cutting. The section was made with a double-bladed knife. During the cutting the scleral rim was used for fixation. In this manner, handling of the corneal tissue itself was avoided.
- 4 A fourth series, of fresh corneas cut out of intact normal rabbit eyes, was used for transplantation in 20 normal rabbit eyes. All frozen-dried material for transplantation was used within ten days to three months after dehydrating, freezing and vacuum packing.

H Method of preservation

The processing of the tissues was done by Drs Paul Weiss and A Cecil Taylor in Chicago as part of project OEMcmr-221 (responsible investigator Dr Paul Weiss). The procedure was essentially the same as that developed for nerves.²

- 1 Excision of donor corneas. The lids were resected, the bulb was fixed in protrusion, washed with sterile Ringer's solution, draped and exposed to radiation from a Westinghouse Ultraviolet Sterilamp (10V-A) at 10 inches (25 cm) for forty-five seconds. The cornea was then excised, as stated in section G.
- 2 Freezing. The excised pieces were immersed directly either in liquid nitrogen (-195°C) or in isopentane chilled to -159°C . No provision was made for equal distribution of the contractile stresses arising in the tissue during freezing, and future experiments should take this point into account. The frozen pieces were transferred to cooled vials, which were then connected with a manifold charged with phosphorus pentoxide and connected with a vacuum pump (pressure, 1 to 5 microns of mercury). Evacuation was continued for four to five days at a

4 Thomas, J W T. The Technique of Corneal Transplantation with Recent Modifications, *Tr Ophth Soc U Kingdom* **57** 520, 1938.

5 Filatov, V P. Transplantation of the Cornea, *Arch Ophth* **13** 321 (March) 1935, in Ridley, F, and Sarsby, A. *Modern Trends in Ophthalmology*, New York, Paul B Hoeber, Inc, 1940.

6 Cuthbert, M. Personal communication to the authors, May 1945.

constant temperature of -38°C and for an additional day at $+20^{\circ}\text{C}$. This treatment eliminates all removable moisture from the frozen tissue.

- 3 Sealing and shipping The vials were sealed by blow torch *in vacuo* at a sufficient distance from the tissues to prevent excessive heating of the latter. The sealed, evacuated vials were then shipped to Philadelphia.

I Methods of rehydration of frozen-dried tissue

The tapering end of the vacuum tube was scratched with a file and a second scratch placed in the belly of the vial. The entire vial was dipped in alcohol for ten minutes, then, after washing in sterile saline solution, the tip was immersed in the rehydrating liquid. The tip was broken off in this fluid, the vacuum sucked the liquid into the vial, and within a few minutes the cornea began to clear. The vial was then broken and the contents poured into a separate container, where the tissue was left for thirty to sixty minutes for complete rehydration. The rehydrating solutions used were Ringer's solution, 0.9, 1.2 and 1.5 per cent solution of sodium chloride, serum and aqueous humor. No difference could be detected in the speed of rehydration or the degree of final transparency with any of these solutions. Isotonic solution of sodium chloride was employed with the majority of eyes.

J Histologic study

Histologic sections of rehydrated rabbit cornea and of healed transplant were made and stained with hematoxylin and eosin and with Mallory's connective tissue stain.

RESULTS

Fifty-nine of the 75 transplanted frozen-dried corneas healed in the recipient corneas. Not one of these 59 grafts was transplanted at any time during the three to six months of observation. In 19 of these 59 grafts corneal vascularization occurred. In 6 of the 59 takes infection was an outstanding and early complication, and in 9 corneal edema persisted. However, in the remaining 25 grafts no complications, such as infection, adhesion of the iris, excessive edema or vascularization, developed (fig. 1).

Of the 16 eyes in which the transplant failed to remain in position, neither lid nor corneal sutures were used in 12. In the remaining 4 eyes corneal sutures were used, and overwhelming infection developed in 3.

In 7 of the 20 eyes that had received fresh corneal tissue for transplantation the graft healed in place and remained transparent for the three to six months of observation. Of the remaining 13 eyes, the transplant failed to take in only 2, in the rest the grafts healed in place but were not transparent. The transplants which failed to remain transparent had one or more of the following complications: corneal edema, vascularization, adhesion of the iris and infection.

Histologic studies of the preserved tissue after rehydration revealed that the stroma differed from the normal in that the nuclei were pyknotic and the stroma was slightly thickened (fig. 3A). The epithelium

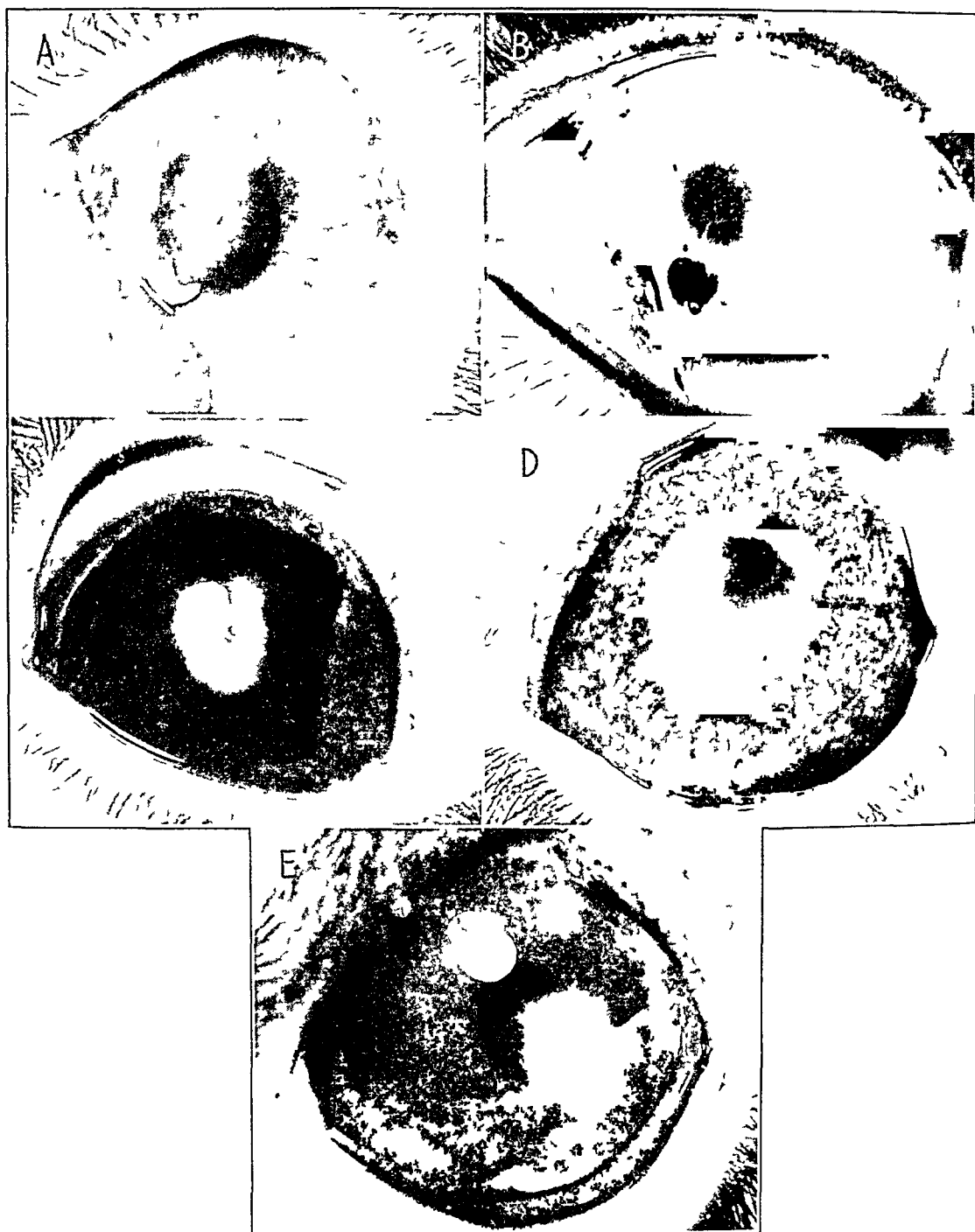


Fig 1—Transplant of frozen-dried cornea cut with trephine, showing *A*, irregular opacification and, *B*, vascularization four months old *C*, five month old transplant of frozen-dried cornea cut with trephine, showing vascularization, *D*, six month old square transplant, the clearest of all transplants with frozen-dried material, *E*, six month old square transplant of frozen-dried cornea, clearing at the edges



Fig 2—*A*, section of healed transplant of frozen-dried cornea, showing irregular lamellae and irregularly thickened epithelium $\times 150$, Mallory connective tissue stain *B*, section of healed transplant of frozen-dried cornea at junction with the host cornea. Connective tissue from the host can be seen passing in front and behind some of the transplant stroma $\times 340$, Mallory connective tissue stain

was present but consisted usually of only two layers. The basal epithelial cells and the directly overlying cells were usually present, the superficial layers having disappeared. Endothelium was intermittently present.

Histologic study of the transplanted but nontransparent frozen-dried corneas disclosed that in all instances the limits of the graft could be determined (figs 2 and 3B). The limit was usually marked by buckling of Descemet's membrane, thickening of epithelium and change in arrangement of lamellae. The endothelium and the epithelium were continuous over almost all the grafts. Some irregularity of stroma could be seen in all sections in the graft area. Occasionally it was difficult to be certain where the stroma of the host ended and the stroma of the transplant commenced. No increase in nuclear content of the stroma or accumulation of inflammatory cells was seen. Some of the grafts showed deep and midstromal vascular invasion. Behind a few of the transplants a new layer of connective tissue had formed. This was not ordinary connective tissue but bore the characteristics of corneal stroma.

COMMENT

The results demonstrate that frozen-dried cornea may be transplanted into normal rabbit eyes without producing an unusual host reaction, that corneal tissue preserved in this fashion is not so altered chemically or physically that it incites an inflammatory reaction in the host.

In an attempt to account for this failure to obtain transparent grafts, several factors must be considered. Rehydration of all preserved corneal tissue prior to transplantation failed to produce clear tissue. All tissue was opalescent or bluish gray regardless of the several rehydrating fluids employed. This finding indicates some change in the preserved corneal tissue which interferes with its normal returgescence. This could be a chemical change. If such a change takes place, it is not one that interferes with healing of the graft, nor does it incite undue inflammatory reaction in the recipient eye. Histologic studies revealed that the stroma of the preserved tissue differed little from normal prior to transplantation, but all sections of healed grafts showed irregular stroma. The disturbance of the epithelium and endothelium, particularly the latter, may account for the opalescence immediately after rehydration and also contribute to the subsequent opacification of the healed transplant. The evidence is not complete as to whether the transplanted corneal tissue persists per se or whether it acts as a framework into which surrounding corneal tissue grows.

The studies of Castroviejo,¹ Imre,⁷ Filatov,⁵ Thomas⁴ and others indicate that successful transparent grafts maintain their individuality

⁷ Imre, J. Clinical and Histologic Studies on Corneal Transplantation, abstracted, *Am J Ophth* **24** 1077, 1941.

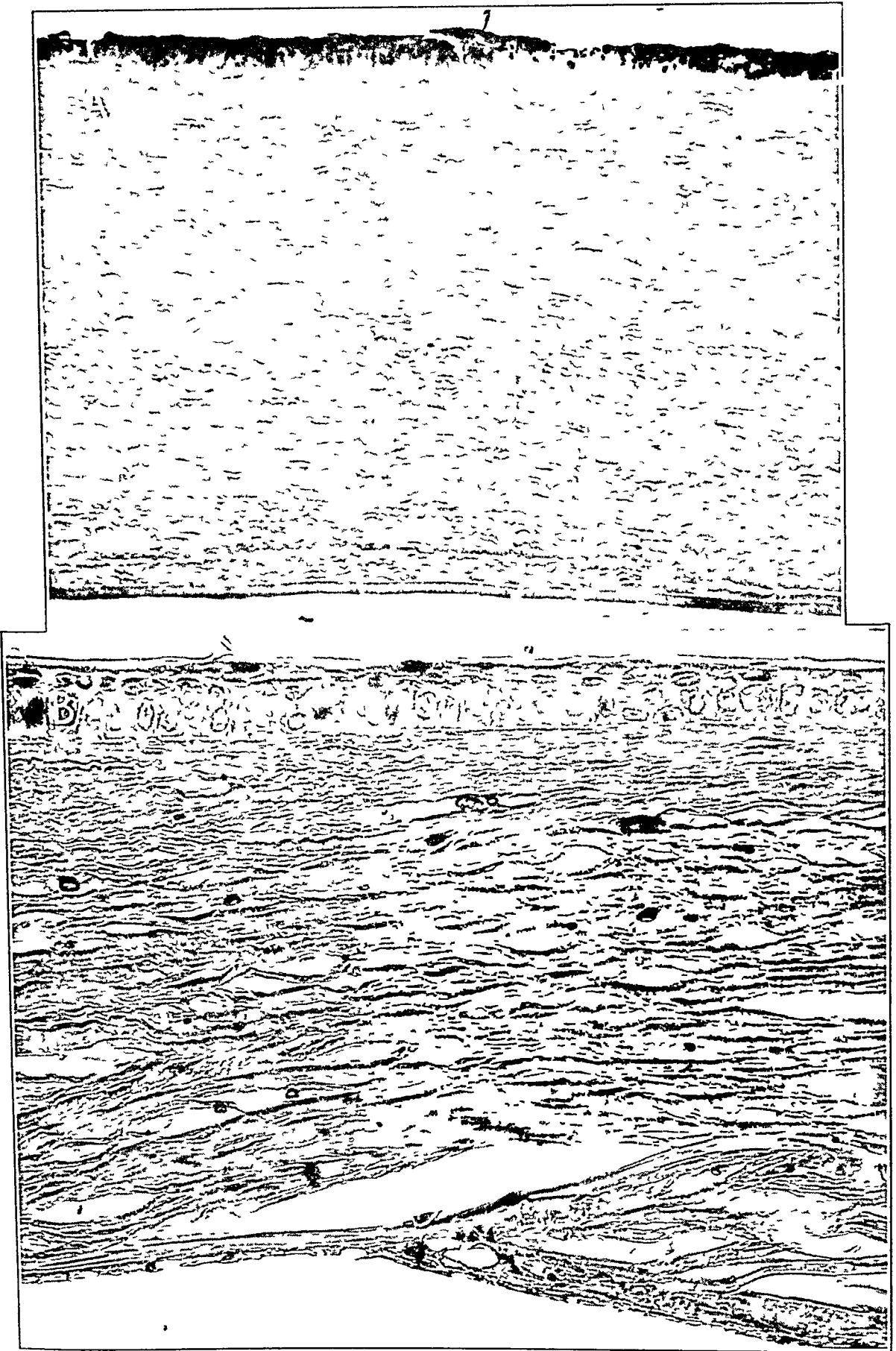


Fig 3—A, section of frozen-dried cornea sixty minutes after rehydration, showing loss of epithelial layers, pyknotic stromal nuclei and intermittent endothelium $\times 170$, hematoxylin and eosin B, section of healed transplant of frozen-dried cornea at junction with the host cornea Descemet's membrane is folded The stroma of the host and that of the graft cannot be easily differentiated. $\times 300$, Mallory's connective tissue stain

and that opaque, nebulous grafts are ones that have been invaded by surrounding host tissue. The studies of Rosenbaum,⁸ Saunders⁹ and Wiener¹⁰ indicate that grafts fixed in a solution of formaldehyde are replaced by the host tissue. The appearance of the majority of serial sections of the frozen-dried corneal transplants suggests that new tissue from the surrounding cornea has replaced, and is replacing, the transplanted tissue.

The impression can also be obtained that replacement occurs only in cases and in areas in which an intimate organic merging of the lamellas of the graft and the host cornea has failed to occur. In the experience of Weiss,¹¹ frozen-dried material varies in this respect.

CONCLUSIONS

Frozen-dried corneal tissue can be transplanted to normal rabbit eyes without an unusual host reaction. However, not one of the 59 takes with frozen-dried cornea were transparent at any time during the six months of observation.

Department of Ophthalmology, Hospital of University of Pennsylvania

8 Rosenbaum, H. Formalinized Heterogeneous and Homogeneous Corneal Transplantations, *Am J Ophth* **25** 731, 1942.

9 Saunders, T., in discussion on Rosenbaum.⁸

10 Wiener, M., and Rosenbaum, H. D. Formalinized Heterogeneous and Homogeneous Corneal Transplantation—Experimental, *Am J Ophth* **24** 1384, 1941.

11 Weiss, P. Personal communication to the authors, Feb 28, 1946.

MODIFIED CORNEAL INCISION WITH IRIDODIALYSIS AND IRIDECTOMY FOR OPENING THE ANTERIOR CHAMBER ANGLE

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WHEN one visualizes the point of attack in making the incision for the conventional iridectomy, one cannot but be impressed with the fact that the very area, namely, the angle of the anterior chamber, which should be kept patent, is in serious danger of being subsequently closed by cicatricial contraction or resultant inflammatory changes as a direct consequence of the location of the incision. The keratome is plunged through a site in proximity to, and probably at times embracing, Schlemm's canal. An area which should be kept free is traumatized, with the possibility of producing conditions worse than the primary one.

The question arises "How can one expect to have a freely draining canal after the cut has been made through or near it and subsequent closure by cicatricial or inflammatory changes has taken place?" It seems to border on the impossible, yet a certain percentage of basal iridectomies bear successful results. Possibly, the favorable outcome in such cases is more good luck than good management. One probably misses the canal in many instances by incising too far forward, in which case a good basal iridectomy is impossible. However, it may not always be so, and though no harm is done, one is still so close to the danger zone that a subsequent inflammatory reaction may complete the picture of obstruction.

In discussing iridectomy, Duke-Elder¹ stated

gonioscopic studies show that the base of the iris is left behind in many cases. Bowman (1862) recommends cutting two pillars of the iridectomy only and tearing the iris away from its root in order to insure its complete removal.

As to the increase in tension after iridectomy, Duke-Elder had this to say²

the base of the iris may not have been resected so that a portion is left blocking up the filtration area, an obstruction often rendered additionally effective by the stump becoming entangled in the wound

Read at the Wills Hospital Clinical Conference, Feb 27, 1946

1 Duke-Elder, W S Text-Book of Ophthalmology, St Louis, C V Mosby Company, 1938, vol 3, p 3401

2 Duke-Elder,¹ p 3302

In the abstract of a paper presented at a meeting of the Section of Ophthalmology, New York Academy of Medicine, Payne³ stated

Ideal postoperative results for the relief of glaucoma are so rarely seen in the laboratory that histologic studies of the material at the New York Eye and Ear Infirmary were made to determine the causes of failure

practically all the sections showed that the operative wound was so far anterior to the normal angle of the iris that a basal iridectomy was impossible. Many of the wounds contained remnants of the iris and ciliary processes and, more rarely, prolapsed crystalline lens. The uveal remains were frequently replaced by dense keloid-like connective tissue, in which evidence of inflammatory reaction remained.

Reese⁴ stated

Microscopic preparations show that most keratome sections for glaucoma are placed too far on the corneal side and that advantage is not taken of the wide margin of safety by making them more peripheral.

It has occurred to me that the failures in some cases of basal iridectomy might be attributed to the aforementioned location of the conventional incision. True it is that the obstructing iris has been removed (or so it is thought), but the drainage is plugged as an after-effect. If this explanation can be accepted, how can consistently beneficial results be expected from any operation which has such a potential danger of defeating its own purpose?

In performing an iridectomy, it is almost impossible, if not quite so, to cut down to the base of the iris without leaving a stump, so to speak, however small. This is a mechanical difficulty. Any remnants of iris can still block the angle.

With these difficulties in mind, I have endeavored to overcome the situation by placing the incision in a location, namely, through clear cornea away from the limbus, where subsequent contraction and other changes would not in any way interfere with drainage. In addition, the location of the incision makes for easy iridodialysis, which, to my mind, is the best manner of clearing out the angle of the anterior chamber.

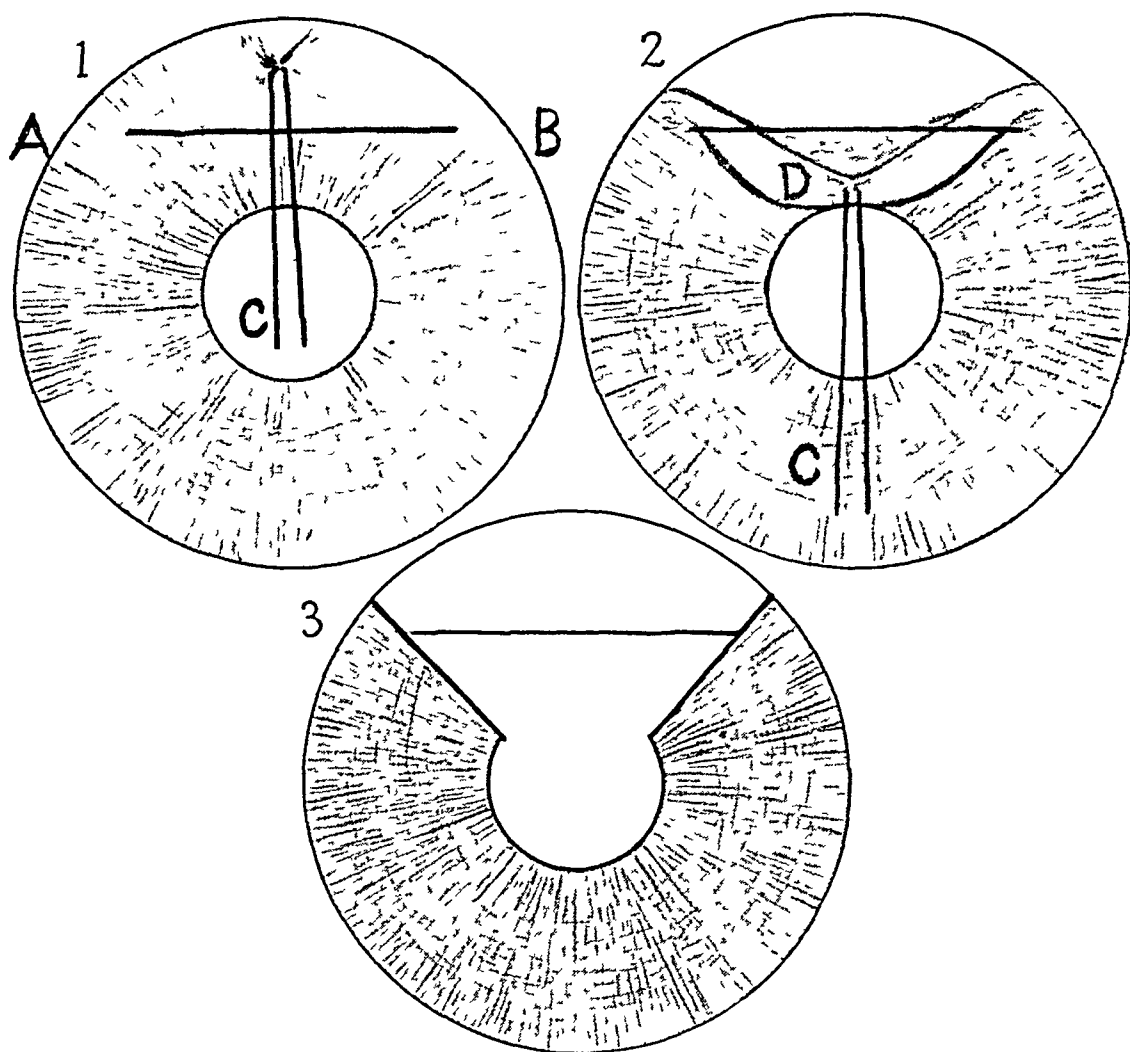
OPERATIVE PROCEDURE

With a Graefe knife, an incision is made straight through and across the cornea about 3 mm below the limbus, with the blade of the knife tilted slightly downward to make a beveled cut. This bevel makes for an easier introduction of the iris forceps, but it should not be excessive or more scar will result.

3 Payne, B. F. Histologic Causes for Failure of Operations for Glaucoma, Arch Ophth 29 518-521 (March) 1943

4 Reese, A. B. The Iridencleisis Operation for Glaucoma, Arch Ophth 34 360-368 (Nov-Dec) 1945

Part of the incision should begin about 2 mm from the outer part of the limbus and terminate at a like distance from the inner part. An iris forceps is introduced through the wound, the operator at the same time lifting gently up on the forceps to avoid any possible injury to the lens. The iris is grasped well up toward the base and pulled slightly downward with a swaying motion, and is stripped clean from its base high up in the angle. The resulting coloboma can be made almost any size desirable. The iris is drawn down and out through the incision.



Technic of performance of iridodialysis and iridectomy through a modified incision in the cornea. In 1, *A* and *B* indicate the corneal incision, and *C* shows the iris forceps grasping the iris. 2 shows the iris pulled through the incision. *D* indicates the iris, and *C*, the forceps. 3 shows the resultant coloboma.

and cut off first at one extremity of the incision, after it has been pulled away medially from the end of the wound, and then at the opposite end. This is important, otherwise, the iris may become wedged in the end of the incision and an anterior synechia result.

In replacing the pillars, the tiny stream of an anterior chamber irrigator is employed rather than a spatula, to guard against any possible

damage to the capsule of the lens. The tip of the irrigator is placed directly against, but not into, the wound, and forcible pressure is applied to the bulb of the syringe. In most instances the pillars of the iris can be easily floated back into place.

After the iridodialysis and iridectomy, free bleeding in a congested eye may occur. Many eyes do not bleed at all. However, one is not concerned with it in many iridectomies, and it is no more serious here. After a few flushings, with a momentary wait between, the bleeding stops. Of course there are cases in which bleeding continues to fill the anterior chamber, but this occurs during iridectomy as well, and one does not think much of it, as absorption takes place later. After the bleeding stops, the eye is bandaged and not opened for two to three days.

My series of cases is not large to date, being about 35, but in no single instance has the iris torn except at the base. At first I was apprehensive lest the iris tear in some unforeseen part, but this has not occurred.

Reese⁵ stated

When the iridodialysis is produced, the iris always tears flush with the ciliary body, leaving no root, because it is here that the iris is thinnest, and also weakest, from the presence of peripheral crypts.

Some may offer an objection to incising through the clear cornea. However, one has only to keep in mind the earlier sections for cataract which healed without trouble, as well as the work done on corneal transplants. Any objection from this standpoint seems to be far outweighed by the fact that anything which will lower the tension is justifiable. The only objection so far as I can see is the tiny linear scar, almost invisible in many cases and above the pupillary area, where it does not obstruct vision.

One may find at times, in the case of an extremely shallow anterior chamber in which the iris is pushed forward and appears to be, or is, in contact with the cornea, that this incision may present difficulties. However, in making an iridectomy in a similar case, thrusting a keratome through the upper part of the limbus and down between the iris, lens and cornea may be just as difficult. One must use his best judgment, as would be in order in any operative procedure. No set operation can be outlined for every situation. One must adapt the proper operative procedure to the conditions obtaining at the time and select the one most fitting to the occasion. As a consequence, I do not advocate the performance of this iridodialysis and iridectomy through the modified corneal incision in every case of glaucoma. It should be employed in any case in which iridectomy might be considered.

⁵ Reese,⁴ p. 363

In the performance of iridectomy, the eye should be thoroughly anesthetized. While the conventional iridectomy does not seem to be a serious operation, it is fraught with danger of injury to the lens should the patient make an untoward movement at the critical time. Also, tearing of the iris by a sudden movement is easily possible, although not a serious complication. The operation I have described calls for the same thorough anesthesia. For some time I have used the retrobulbar injection of 2 per cent procaine hydrochloride in all my iridectomies, and of course I employ it in this procedure. In addition, to be doubly safe, I inject a small amount of the anesthetic subconjunctivally, to form a bleb, just above the upper portion of the limbus. One must have a quiet eyeball when such delicate work is done, and anything which favors this status should be made use of. Too many cataractous lenses give mute evidence of poor anesthesia or unfortunate technic during the performance of iridectomy.

I am not suggesting this procedure of iridodialysis and iridectomy with the thought that all high tensions can be reduced, as too many other factors enter into the situation, especially in cases of chronic glaucoma with obliteration of the angle. However, I feel that the operation offers a better means of securing a broad coloboma with a clean angle and that the suggested location of this incision makes for its easy accomplishment.

HEMIFACIAL SPASM

Report of Two Cases

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NEW YORK

HEMIFACIAL spasm is a condition in which the patient has paroxysms of twitchings in muscles innervated by the seventh nerve. The condition is not under voluntary control and defies mimicry. It imitates the effect of faradization of the facial nerve and characteristically involves one half of the face. Cases of bilateral spasms¹ have been reported. In the latter a different mechanism is apparently operative, and most of the cases reported have been associated with paralysis agitans. Cases have also been reported in which first one side was involved, with a remission, only to be followed by involvement of the other side. The condition has also been called facial hemispasm, but when one half of the face is involved the term hemifacial spasm is more correct.

Hemifacial spasm is not a tic. According to A. Gordon,² a tic is a sudden and abrupt contraction of one or several of the muscles of the face. The contraction is always the same as to range and location, but the invaded area does not correspond to a well defined anatomic distribution of a certain nerve, as in spasm. Tic has a tendency to spread and invade other functions, so that at the time of the grimace the tongue may be protruded, or there may be a laryngeal cry. Tic can be controlled to a certain extent and is an exaggeration or disfigurement of physiologic gestures or mimicry, and may be psychogenic.

Spasm is the opposite of the normal physiologic course of events. Normally, when one eye closes voluntarily, the corresponding brow descends. In spasm the inner part of the brow is elevated at the moment the eye begins to close. The forehead is wrinkled, the palpebral orbicularis closes the eye, there is simultaneous contraction of the frontalis and orbicularis muscles, the zygomatic muscles deviate the angle of the mouth, and, according to the mode of muscular contraction,

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1. Parker, H. L. Bilateral Facial Spasm, *Am J Ophth* **16**: 28 (Jan.) 1933.

2. Gordon, A. Convulsive Movements of the Face, *J A M A* **58**: 97 (Jan. 13) 1912.

the angle is either drawn laterally or elevated. The nose is curved to the affected side, and the chin on this side shows a characteristic depression. One sees coarse contractions of wide range occurring in either the upper or the lower branches of the seventh nerve. Both branches may be involved, and when the lower is included there may be involvement of the muscles of the neck. In some cases fine contractions are seen. The spasm occurs during sleep and is not broken by will. Spiller expressed the belief that the movement is always an associated one, for example, the eyelids may move with the mouth.

The condition is not common, especially in the American literature.

Parker¹ cited Meige as stating that all his patients were of more than middle age and were of relatively stable personality. In all of Meige's cases the spasm was bilateral, and since it started in the eyelids the patients were blinded during the spasm. It has been characteristically noted in most cases of hemifacial spasm that the first portion of the face to be involved is the orbicularis muscle, so that the patient will frequently first present himself to an ophthalmologist complaining that his eye is becoming smaller. Later, other muscles in the distribution of the seventh nerve are involved. The spasm is usually clonic but may become tonic.

Ehni and Woltman³ recently reviewed 106 cases from the Mayo Clinic. The age distribution was from 17 to 70, 60 per cent of the patients being females. In their series, 65 per cent of the patients described the spasm as beginning in the lids, and in 90 per cent the muscles of the eyelids were involved early in the course of the disease. These authors were unable to account for the early and frequent involvement of the eyelids, unless it is, as Gowers has stated, that the "motor mechanism of this muscle is more sensitive, in consequence of its energetic reflex action." In 104 of their 106 patients the lids were involved. They described the spasm as being of a twitching nature, an intermittent and irregular series of single muscle twitches, coming in rapid sequence and involving but a fraction of the muscle fibers of any one muscle in any one twitch. Twenty-one patients had both twitches and sustained spasm, and in most of the attacks the twitchings increased periodically in frequency and intensity until, at the climax, there was a sustained spasm, lasting from a few seconds to a minute. Some had sustained spasm lasting five minutes.

Only 3 of their patients had had a preceding Bell's palsy, and in 2 of these the spasm was on the same side. Twenty per cent of their patients were aided by solitude, pressure below the lobe of the ear, relaxation and rest. Nine had had periods of freedom of up to three years.

³ Ehni, G., and Woltman, H. Hemifacial Spasm, *Arch Neurol & Psychiat* 53: 205 (March) 1945.

These authors summarized the pertinent points in the diagnosis as follows

- 1 The spasms are of an intermittent twitching nature, such as might be encountered in intermittent faradization of the nerve
- 2 The eyelids on the side of the spasm are almost always involved
- 3 The spasms are usually unilateral, and when they are bilateral they are not synchronous or equal in extent or severity
- 4 The spasms may persist in sleep
- 5 The patient does not feel any compulsion to make the movement
- 6 The patient is unable to stop the movement by exertion of the will
- 7 The patient cannot reproduce the movement voluntarily—especially is he unable to approach the speed with which fine twitchings occur.
- 8 Psychic upsets of any sort, fatigue and voluntary movements of the face make the spasms worse
- 9 Children do not have hemifacial spasm
- 10 The spasms are limited to the muscles innervated by the facial nerve

CAUSE AND MECHANISM OF THE SPASM

The actual cause of the hemifacial spasm is unknown. The majority of writers on the subject feel that in most cases the spasm is due to some peripheral irritation, nevertheless, an irritation of any segment of the reflex arc (of the seventh or of the seventh and fifth nerves), as well as organic lesions higher up in the cerebrum, may be considered etiologic. Disorders of the teeth, meningoencephalitis, encephalitis, neuromas, injuries and toxic neuritis of the seventh nerve, and conjunctivitis are among the many conditions which have been considered causative. I have already noted that the condition not infrequently occurs in association with paralysis agitans.

From an etiologic point of view it would seem that hemifacial spasm should be divided into two types—one due to, or following, injuries to or lesions of the seventh nerve, and the other on an apparently idiopathic basis. It is of interest that in my first case, which at this moment falls under the idiopathic type, there should be electroencephalographic evidence of encephalitis. It should be interesting to note the findings in studies of the electric potentials of the brain in a larger series of cases.

In the type which follows Bell's palsy due to toxic neuritis or trauma, as in my second case, the mechanism is more obvious, even if not completely clear.

Spiller⁴ in 1919, in referring to the latter type, expressed the belief that during regeneration of the damaged nerve axis-cylinders intended

4 Spiller, W. Contracture Occurring in Partial Recovery from Paralysis of the Facial Nerve and Other Nerves, *Arch Neurol & Psychiat* 1: 564 (May) 1919.

for the upper branch of the seventh nerve wandered into the lower branch, and vice versa. "The muscles on the affected side, as a result of this excessive stimulation, are kept in a state of hypertonicity and contracture results." Fowler⁵ did not agree with this and as a result of his experimental work on monkeys came to the conclusion that there is a splitting of the neurofibrils at the point of repair. He stated that the individual axons pass into the neuroma (at the site of the injury) and break up into neurofibrils, which run in every direction. If the latter happen to encounter peripheral branches of the severed nerve, they may enter these various branches. Thus, a single axon may send out neurofibrils some of which get lost in the fibrous tissue of the neuroma and others reinnervate distal branches which belong to the neck, lip, nose or forehead, or conceivably all of these regions. If any type of impulse reaches the medullary cell belonging to this axon, it produces movement of several of the facial muscles. Fowler showed that in cases of injury to the facial nerve, if the injured nerve was isolated and severed, stimulation of the distal stump with a mild faradic current proved that the branch might innervate only a nearby, highly localized area, but if the proximal end was so stimulated there was invariably produced movement of the entire face, scalp and platysma muscle. The latter phenomenon did not occur on the uninjured side.

After operations in the area of the seventh nerve, if the typical spasmodic contractions are present, it may be assumed that injury and repair have taken place. Ernest Sachs, in his discussion on Fowler's paper, cited Dustin's old experiments to show that in regeneration of the fifth nerve one could not make the axis-cylinder hook up with the branch from which it had originally been separated.

Howe, Tower and Duel,⁶ writing on the same subject, stated

it remains to be shown that a single axon can normally supply fibers to two distinct muscles or to spatially separate portions of the same muscle. There is abundant evidence that under pathologic conditions one axis-cylinder may arborize over a wide area.

They expressed the belief that in experimental animals at least, the gravity of the twitch was in direct proportion to the degree of disturbance in the bed of the nerve, rather than to the amount of the paralysis. They found the severest spasms after nerve section, whereas freezing or injection of alcohol gave a less severe result.

Injury and repair of a nerve trunk, such as the facial nerve, give an opportunity for peripheral confusion of two sorts. Either nerve fibers, totally misdirected in regeneration, may come to supply muscles with which no original connection

5 Fowler, E. P., Jr. Abnormal Movements Following Injury to the Facial Nerve, *J. A. M. A.* **113** 1003 (Sept 9) 1939.

6 Howe, A., Tower, S., and Duel, A. Facial Tic in Relation to Injury of the Seventh Nerve, *Arch. Neurol. & Psychiat.* **38** 1190 (Dec.) 1937.

existed, or, by branching, one regenerated axis-cylinder may innervate a large portion of the facial field

The physiologic and the anatomic evidence thus agree in demonstrating the presence of branching axons in the regenerated facial nerve, and the physiologic evidence shows further that branches of one axon may be distributed to innervate portions of the facial musculature as far apart as the frontalis and the nuchal platysma muscle. This condition provides an adequate basis for the mass contractions—the so-called facial tics—which follow on injury to and repair of the facial nerve in the experimental animal. However, whether or not this is the entire mechanism of the posttraumatic tic is undetermined, since there remains the possibility that during regeneration nerve fibers which originally supplied one muscle become totally misdirected to supply quite another muscle and yet still act when the original group is brought into play.



Fig 1—*A*, patient as he appeared at first examination. Note the narrowed right palpebral aperture, pronounced nasolabial fold and depression in the right side of the chin. *B*, appearance on opening the mouth. There is no evidence of palsy. *A* and *B* show the compensatory widening of the left palpebral fissure. *C*, both eyes closed.

These same authors added one prognostic point, that is, that in their monkeys the spasm showed no diminution over a period of three years, and expressed the belief that there was no basis for belief that any further modification would take place.

I present 2 cases of hemifacial spasm, 1 of the idiopathic type and the other of the type seen during the regeneration of a damaged seventh nerve (post-Bell-palsy).

REPORT OF CASES

CASE 1—C. D. (fig 1), a white man aged 27, was admitted to the ophthalmic clinic of the New York Hospital on April 11, 1945, complaining that his right eye was getting smaller. He dated the onset of his condition to some time in 1942, when, after recovering from a "cold," his mother called his attention to the fact that his "right eye looked smaller than the left." There was no

associated pain or headache. He said that diplopia was present only "when I read a paper too long." He stated that the application of heat opened the right eye a small amount. He had noted no remissions and no change in his speech.

His past history was irrelevant except for rheumatic fever in childhood. He was said to have a "rheumatic heart" and noted dyspnea on marked exertion.

Examination revealed an apparently healthy man with a "Janus-faced" appearance. The right palpebral aperture was greatly narrowed vertically and horizontally. In the primary position the vertical measurements were 5 to 6 mm for the right palpebral aperture, as against 14 mm for the left. The latter was wider than normal, and it was felt that this was on a compensatory basis. Horizontally the apertures measured 28 mm on the right and 35 mm on the left. With the Hertel exophthalmometer set at 105 mm, the readings were 15 on the right and 17 on the left.

There was pronounced facial asymmetry, with movement present on both sides of the face. The right nasolabial fold was prominent, and the mouth and nose were drawn to the right. Both sides of the forehead were wrinkled, and fairly equally so. There was a marked depression in the right side of the chin. This appearance of his face was constant, and no actual spasmodic contractions were noted. Vision was 20/20 in the right eye and 20/15 in the left eye. It was felt that the difference in vision was on the basis of the narrowed aperture.

The right palpebral fissure had an epicanthoid fold at the external canthus. The right lower lid reached to within 15 mm of the pupil. The pupils reacted to light and in accommodation. The conjunctival and corneal reflexes were present but were questionably decreased on the right. The extraocular motility was difficult to evaluate because of the difference in size of the fissures, but apparently there was a double paresis of the elevator muscles on the right, with weakness of both inferior and both external rectus muscles. The near point was 80 to 90 mm. There was no diplopia in the primary position either for far or for near vision. There was diplopia in all fields with the red glass. This was greatest to the right and up and to the right. On the right side the diplopia was crossed, on the left, homonymous. There were nystagmoid movements in lateral gaze.

The pupils were equal in size. Facial perspiration was equal on the two sides. Photographs taken in 1937 showed no abnormality of the face. A photograph on his badge, taken in 1944, showed a condition much the same as that seen during his examinations here.

The patient was admitted to the hospital for further study. Observations made during sleep and during sleep under heavy narcosis revealed no change in the appearance of the face, the spasm persisting. Procainization of the right facial nerve at the stylomastoid foramen caused complete facial palsy on the right and did not reveal the presence of any permanent tissue contractures except those of the nasolabial fold. The red glass test showed no change.

Roentgenograms of the skull and orbits revealed no pathologic condition. The fields were normal. Examinations of the blood, urine and spinal fluid all showed an essentially normal condition.

The heart was enlarged, and there were a systolic and a diastolic murmur. The blood pressure was 130 systolic and 80 diastolic. The electrocardiogram confirmed the diagnosis of rheumatic heart disease. Electroencephalographic study showed "a pathologic record revealing a diffuse abnormality, with a probable right occipital focus. The nature of the abnormality was not indicated." The possibility of encephalitis was considered.

Neurologic examination by Dr Henry Dunning revealed nothing of note other than the changes already described in the face.

The patient was desirous of having surgical correction of the deformity and felt that even a facial palsy was preferable to his condition. Accordingly, he was later readmitted to the hospital, and on Sept. 28, 1945 Dr Bronson Ray performed a partial division of the right facial nerve for the relief of the hemifacial spasm.

The operation itself and the observations made during it are so interesting that I am including the more pertinent portions of Dr Ray's operative summary.

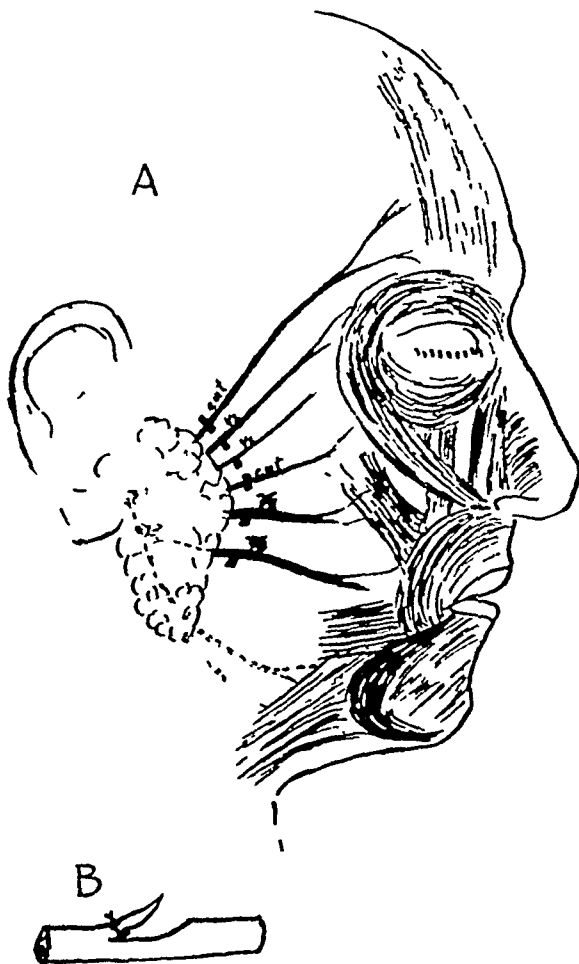


Fig 2—Dr Bronson Ray's drawings of the surgical procedure in case 1. *A* shows the branches of the seventh nerve as they were exposed during the operation. The thickness of the cross hatching indicates the relative depths of the incisions into the branches. *B*, method of partial division of the nerve and ligation of the proximal slip to prevent regeneration.

"This patient's problem has been an interesting one. He is a young man of fairly stable nature who for three years has had uncontrolled spasmodic twitch of the right side of the face. The twitching involves all parts of the face supplied by the facial nerve, but most of all the orbicularis oculi, the twitching of the latter being of such degree that vision was impaired because of the frequent blinking. It appeared almost that there was some permanent contraction of the muscles, particularly those forming the nasolabial fold. On two occasions the

facial nerve was procainized at the stylomastoid foramen, producing complete facial palsy. At such times it was seen that there was indeed some degree of contracture of the muscles mentioned, because the nasolabial fold persisted. The patient was anxious to have some effort made to relieve the spasm, even though complete palsy was the only solution. I was anxious, in his case, to try what I have not heretofore had the opportunity of doing, namely, partial division of the branches of the facial nerve. German⁷ has reported several cases in which he performed this operation, and, in my personal conversation with him, he expressed the opinion that the method had advantages. In addition to the initial satisfactory results of this operation, today, it is interesting to note the results of electrical stimulation of the nerves."

As a prelude to the actual operation, the facial nerve was exposed, uncovering two fair-sized branches and four smaller ones. It was felt that all the branches were exposed in the area of the parotid gland. The lowest branch appeared to

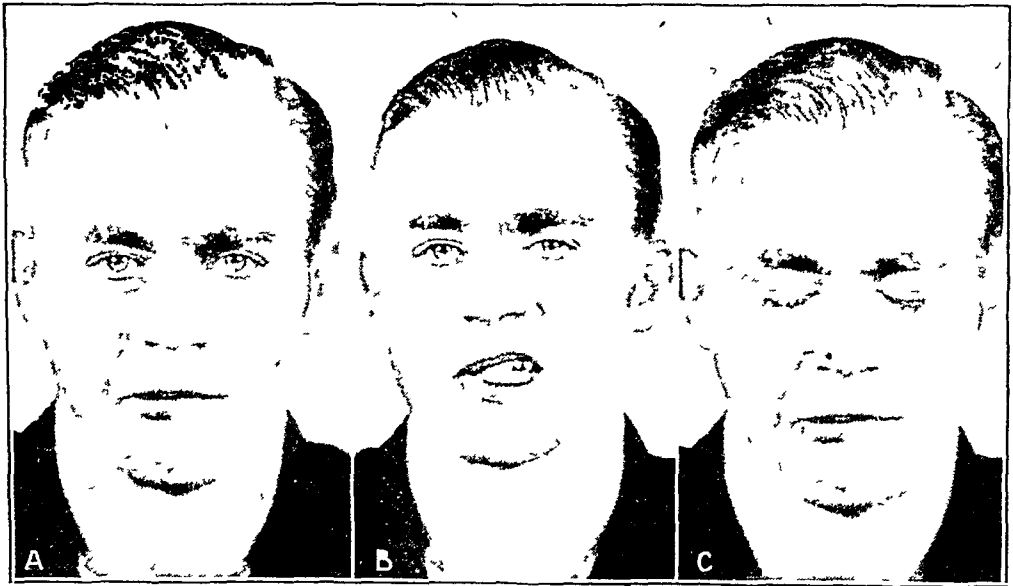


Fig 3—Postoperative appearance of patient shown in figure 1. The palpebral fissures are of same size. The nasolabial fold and the depression in the chin are still present.

supply the upper lip and the upper angle of the mouth. The middle branch supplied the muscles of the cheek and the maxillary area along the nasolabial fold. The four smaller branches supplied the orbicularis (lower part), the angle of the eye, the orbicularis (upper part) and the muscles of the forehead. Stimulation of these branches with a current of 2 volts, using the Hinsey-Geoghegan stimulator, produced such discomfort that it was necessary to lower the current to a minimum. When the current was cut down to nearly zero on the ammeter and the nerve was touched with only one of the bipolar electrodes, the patient received a shocklike, stinging sensation in the localized region which each branch presumably supplied. He could successively and repeatedly identify the location of the pain experienced when various branches of the nerve were stimulated. This would appear to indicate that the facial nerve has pain fibers, but unless

⁷ German, W. J. Surgical Treatment of Spasmodic Facial Tic, *Surgery* 11:912 (June) 1942.

the trigeminal nerve was paralyzed simultaneously no such conclusion could be drawn

After the examination with the stimulator, each branch of the facial nerve was divided one-half the way through This was done by introducing a short



Fig 4 (case 2) —*A*, patient's usual appearance Note the narrowed right palpebral fissure *B*, attempted greater opening of the eyes, resulting in the opposite effect *C* and *D*, profile views taken at the same time as *A* and *B* *E*, one week after procainization of the seventh nerve and during the period when there was a remission of symptoms

bistoury blade into the nerve, with the blade running parallel with the fibers. The blade was then carried along the fibers and turned outward with a clamp, while a silk ligature was placed around its base. This was for the purpose of preventing regeneration (fig 2).

When the patient was then undraped, it was noted that the major part of the spasmodic contractions had stopped. There was some residual twitching in part of the superior portion of the orbicularis and along the upper margin of the lip, in an area extending into the nasolabial fold. It was thought desirable to divide more fibers to abolish the remaining elements of spasm about the eye and the upper lip. Hence, two of the four uppermost nerves were completely severed and ligated, and the incisions in the two lower branches were deepened to about two thirds of the way across.

Immediate postoperative examination revealed weakness of the muscles of the forehead and the upper part of the face, but the distortion was not serious. The palpebral apertures were of equal size, and the eyes could be closed equally. A small spasmodic twitching was still apparent in the chin and the lower lip. While this had been present before, it was now more apparent, in contrast to the rest of the face.

Figure 3 shows the patient as he appeared about ten days after operation.

CASE 2—Mrs J D (fig 4), a white woman aged 65, was admitted to the department of otology of the New York Hospital with the complaint of pain in her right ear, associated with a discharge. Her present illness dated back two years. She also stated that she had had "noise like a train" in that ear and mild pain in the region of the right internal canthus. She had had a mastoidectomy on the right side in another hospital in August 1944, followed by Bell's palsy on that side and accentuation of the pain about the eye. There was no amelioration of the aural symptoms and discharge. There had been a pronounced and progressive decrease in the Bell palsy, but she noted that her right eye "was becoming smaller." She complained of cramps about this eye, lasting several minutes, during which her eyelids had become partially or completely closed, thus interfering with vision. There was no diplopia. She also experienced pain in her right shoulder and arm.

The patient had had sciatica on the right side for twelve years, with two unsuccessful attempts at surgical treatment.

Physical examination revealed obesity. The patient had a marked language difficulty and tended to say "yes" in response to all questions. There was a facial asymmetry with palsy of the right side of the face, drooping of the right corner of the mouth and pulling of the mouth to the left. The right palpebral aperture was greatly narrowed, and attempts to open the eyelids wider only resulted in greater spasm in the orbicularis than was already present. The forehead was wrinkled bilaterally. At times there was more pronounced narrowing of the right palpebral aperture, associated with coarse spasmodic twitchings. These were transient, lasting from several seconds to several minutes. The pupillary reactions were normal. The conjunctival and corneal reflexes were present and questionably diminished bilaterally. The tongue protruded in the midline and was without tremor. There was a scar of an old mastoidectomy on the right. Audiometer readings showed 61.3 per cent deafness in the right ear and 31.3 per cent in the left ear. There was some vertigo on sudden movement. Neurologic examination otherwise revealed an essentially normal condition except for some weakness of the right leg. Vision was 5/100, with correction to 20/30 in each eye. The fundi were essentially normal for a person

of her age. Roentgenograms of the mastoids showed a postoperative condition on the right and a normal mastoid on the left. Roentgenograms of the skull showed "hyperostosis frontalis and a moderate amount of calcification of the internal carotid arteries." The chest was normal except for elongation of the aorta. There was generalized hypertrophic arthritis of the spine. Laboratory tests, including hemocytologic studies, urinalysis, serologic determinations and examinations of the spinal fluid, gave normal results. Procainization of the supra-orbital nerve did not relieve her pain, but a similar injection at the site of the supratrochlear nerve caused immediate cessation of the pain in the eye, lasting for about two hours. Lid block caused the palpebral apertures to assume the same width. On December 18 an attempt was made to procainize the right seventh nerve at the stylomastoid foramen. This was repeatedly unsuccessful. It was repeated at the condyle and was successful in producing a complete palsy, lasting about fifteen minutes. She returned nine days later and stated that she had been free from the facial spasm for four days. At the time of her return visit there was a difference of only 2 mm between the two fissures (right, 8 mm, left, 10 mm), whereas usually there was a difference of 4 to 6 mm. At present she has no evidence of palsy on the right, but the spasm is still present. The aural discharge has cleared under treatment, although there is a perforation of the right drum membrane.

TREATMENT

Practically every form of artificially produced paralysis of the seventh nerve has been utilized in the treatment of this spasm. The treatments fall essentially into three categories: sedation, injection of alcohol or some local anesthetic into the nerve and surgical intervention. Most of the surgical procedures have been in the direction of anastomosis of the distal portion of the seventh nerve with one of the other cranial nerves. The procedure used on my first patient would seem to be a simpler and more rational procedure.

DIFFERENTIAL DIAGNOSIS

The diagnosis of hemifacial spasm is comparatively simple if it is recognized that the condition is one of spasm. It must be differentiated from facial hemiatrophy. The latter, like spasm, gives a "Janus-faced" appearance, but the pathologic process is one of atrophy of all the tissues of one side of the face, with a "falling in" of the facial structures. At least one member of the house staff failed to recognize the presence of spasm in the woman who had had Bell's palsy and made a diagnosis of paralysis of the seventh nerve of the upper motor neuron type.

Spasm may be due to neoplasm or disease along the course of the nerve or in the posterior fossa and can be excluded by the other signs of these lesions. True tic tends to involve other nerve distributions and is variable and psychogenic. The history of Bell's palsy differentiates this condition from the idiopathic form.

Williams⁸ has described a series of cases of a condition resembling hemifacial spasm in which head turning was also present and in all of which the disorder was on the basis of psychic trauma and responded to psychotherapy. In all these cases the history pointed to the psychogenic factor.

COMMENT

It is unfortunate that many of the authors on this subject use the term "tic" when they mean "spasm." The term "tic" should be reserved for grimaces of a psychogenic nature or for grimaces which have become a habit. Some authors have indicated that the cases of spasm following Bell's palsy fall into a different group. It would seem that when there is a true, uncontrollable spasm of one-half the face the term "hemifacial spasm" is indicated, the fact being borne in mind that etiologically there are at least the two types of hemifacial spasm—the one idiopathic and the other following trauma or infection of the seventh nerve.

There has been some confusion in the use of the terms "spasm" and "contracture." I feel that the term "contracture" implies tissue changes which tend to hold the structures in a distorted form, which may increase and which do not disappear under procainization.

Woltman and Ehn¹ stated that the lesion does not apparently extend distal to the exit of the seventh nerve at the stylomastoid foramen, as section here and anastomosis result in reinnervation of the face with no recurrence of the twitching.

My first case is unusual in that the patient had an apparently sustained spasm. The involvement of the extraocular muscles suggests encephalitis as the etiologic factor.

SUMMARY

The condition of hemifacial spasm is described and attention called to the fact that at least two forms exist—one on an idiopathic basis and the other following regeneration of a traumatized seventh nerve. An illustrative case of each is presented.

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⁸ Williams, T. A. Mechanism of Some Convulsive Movements of the Orbicularis and of the Face, *Arch. Ophth.* 5:272 (Feb.) 1931.

COMPLETE UNILATERAL OPHTHALMOPLÉGIA DUE TO PRIMARY CARCINOMA OF THE SPHENOIDAL SINUS

Sphenoidal Fissure-Optic Canal Syndrome with Complete Ophthalmoplegia,

Report of a Case

I S TASSMAN, M D

PHILADELPHIA

A NEOPLASTIC, inflammatory or traumatic process which involves the structures passing through the sphenoidal (superior orbital) fissure and the optic canal may result in pressure on these structures and cause an ophthalmoplegia. The condition has been described in the literature as the "orbital apex-sphenoid fissure syndrome." The important structures which pass through the sphenoidal fissure are the third, fourth and sixth cranial nerves, the three branches of the ophthalmic division of the fifth nerve, the ophthalmic vein, the orbital branch of the middle meningeal artery (when it does not pass through the middle meningeal foramen) and the sympathetic fibers from the cavernous plexus, the sympathetic root of the ciliary ganglion, and (sometimes) the sensory root of the ciliary ganglion. In a roentgenographic study of 370 cases by Guidotti,¹ the sphenoidal fissure was found to show many anatomic variations, and he stated that it is not always possible to distinguish satisfactorily by roentgenogram between the normal and the abnormal case.

The optic nerve, the ophthalmic artery, branches of the sympathetic carotid plexus and the orbital prolongations of the meninges which form the sheath of the optic nerve pass through the optic canal. The structures primarily involved in the complete syndrome are the second, third, fourth and sixth cranial nerves, the ophthalmic division of the fifth nerve, sympathetic fibers, the ophthalmic vein and the ophthalmic artery. The syndrome is considered to be incomplete when the optic nerve or some of the other structures are spared. An analysis of the cases previously reported would seem to indicate that only those in which the ophthalmoplegia is complete should be considered as true cases of the syndrome. Moreover, the term "orbital apex-sphenoidal fissure

Read before the College of Physicians of Philadelphia, Section on Ophthalmology, Feb 21, 1946. A discussion of this article appeared in the August 1946 issue of the ARCHIVES, pages 246-247.

1 Guidotti, C. L'aspetto radiografico della "fissura orbitalis superior," Radiol med 24 1074 (Dec) 1937.

syndrome" does not appear to be specific for or descriptive of the condition. It indicates in a general way the site of the lesion, but, like the name of many other syndromes, it fails to provide any idea of the symptom complex. It would seem better to designate the syndrome as a complete ophthalmoplegia and to indicate that it is due to disease simultaneously involving the sphenoidal fissure and the optic canal, rather than the orbital apex. The name "sphenoidal fissure-optic canal (S-O) syndrome with complete ophthalmoplegia" would accomplish this.

About 10 cases of the syndrome have been reported in the American literature since 1900. In 1940 Holt and de Rotth² published an excellent review of the subject and reported 4 of their own cases under the title "orbital apex-sphenoid fissure syndrome." They pointed out the importance of the condition to the ophthalmologist and stated that no case had previously been described in the American ophthalmic literature. The first typical case in the American literature was reported by Hunter³ in 1900, the syndrome being due to a gumma at the apex of the orbit. Landman⁴ described a case in 1907 in which the optic nerve was spared. Other cases were reported by Finlay,⁵ Jackson⁶ and Ré and Muhlmann,⁷ and several in the South American literature, by Ayala Haedo and de Ayala Haedo⁸ and by López Villoria.⁹ In the French, German and British literature not more than about 100 cases of this syndrome have been reported since 1861.

The syndrome was described as the "sphenoid fissure syndrome" in 1896 by Rochon-Duvigneaud.¹⁰ However, Rollet, in 1865, called attention to the occurrence of ocular paralyses with syphilitic periostitis of

2 Holt, H., and de Rotth, A. Orbital Apex and Sphenoid Fissure Syndrome, *Arch Ophth* **24** 731 (Oct) 1940

3 Hunter, D. W. A Case of Gumma of the Apex of the Orbit, *New York Eye & Ear Infirmary Rep* **7**:17 (Dec 7) 1900

4 Landman, O. A Case of Monocular Ophthalmoplegia Interna and Externa with Paralysis of the Abducens and Trochlear, *Arch Ophth* **36**:367, 1907

5 Finlay, C. E. Two Cases of Syphilitic Lesions Situated at the Sphenoidal Fissure. Sphenoidal Fissure Syndrome, *South M J* **23** 51 (Jan) 1930

6 Jackson, J. De W. Unilateral Ophthalmoplegia Totalis Probably Due to Encephalitis Lethargica, *Pennsylvania M J* **33** 161 (Dec) 1929

7 Ré, B. V., and Muhlmann, V. Síndrome de la hendidura esfenoidal curodo, *Semana méd* **2** 240 (July 27) 1933

8 Ayala Haedo, A., and de Ayala Haedo, L. R. Un caso de síndrome del ápice orbitario y síndrome paratrigeminal del simpático ocular, *An oftal y otorino-laring d Paraguay* **3** 186 (Aug) 1941

9 López Villoria, L. Síndrome de la hendidura esfenoidal y parálisis facial por un sarcoma de la parótida, *Arch venezol Soc de oto-rino-laring, oftal, neurol* **2** 68 (June) 1941

10 Rochon-Duvigneaud, A. Quelques cas de paralysie de tous les nerfs orbitaires (ophthalmoplegia, totale avec amaurose et anesthésie, dans le domaine de l'ophtalmique d'origine syphilitique), *Arch d'opht* **16** 746 (Dec) 1896

the sphenoidal fissure, but he did not consider this a clinical or pathologic entity. In 1927 Dejeans¹¹ reported 5 cases, with a complete review of the literature. According to Dejeans, the first case in which the syndrome was due to a tumor of the sphenoid bone was reported by Dinkler in 1891.

In 1935 Roger and Alliez¹² also reviewed the literature and collected 50 cases, excluding those in which the syndrome was attributed to traumatism and infection of the sinuses. It was due to neoplasm in 20 cases and to syphilis in 16 cases. Of 15 cases of their own, the syndrome was said to be caused by neoplasm in 7. Cancer of the sphenoid bone was present in 2 cases, metastatic tumor, in 4 cases with the primary growth in the breast, kidney, lung and intestine, and a disseminated epithelioma of unknown origin, in 1 case. Cases of tumor occurring in the neighborhood of the sphenoidal fissure and in the sphenoid bone without any signs of the syndrome have also been described by Herzau¹³ and by David and Hartmann¹⁴.

Carcinoma of the sphenoidal sinus is uncommon. Salinger,¹⁵ in his excellent review of the paranasal sinuses, cited Bach,¹⁶ who stated that the literature recorded 40 cases of malignant tumor of the sphenoidal sinus, in only 10 of which the tumor was carcinoma. This small number was explained by the fact that such a tumor is seldom diagnosed early enough to establish definitely the point of origin. Other cases have been reported since 1938 by Hardie and Ahronheim¹⁷ and by Tolan.¹⁸ The latter stated that carcinoma of the sphenoidal sinus has five routes of extension. In order of frequency, these are orbital, nasal, cranial, petrous and occipital. The case which they presented was an example of the last and was believed to be the only one of this kind on record.

The symptoms usually complained of in the sphenoidal fissure-optic canal syndrome are hyperesthesia or anesthesia of the upper lid, half

11 Dejeans, C. Les syndrome paralytiques du sommet de l'orbite, *Arch d'opht* **44** 657 (Nov) 1927.

12 Roger, H, and Alliez, J. Etiologie des syndromes de la fente sphénoïdale et de l'apex orbitaire. Efficacité du traitement antisiphilitique, *Rev d'oto-neuro-opht*. **13** 245 (April) 1935.

13 Herzau, W. Zur Klinik der ein- und doppelseitigen Ophthalmoplegien peripheren Ursprungs, *Arch f Ophth* **125** 207, 1930.

14 David, M, and Hartmann, E. Les symptômes oculaires dans les méningiomes de la petite aile du sphénoïde, *Ann d'ocul* **172** 177 (March) 1935.

15 Salinger, S. The Paranasal Sinuses, *Arch Otolaryng* **30** 442 (Sept), 633 (Oct) 1939.

16 Bach, S. Carcinoma primitivo del seno sfenoidal, *Valsalva* **14** 390 (Aug) 1938.

17 Hardie, G C, and Ahronheim, J H. Primary Carcinoma. Left Sphenoid Cavity, *Arch Otolaryng* **38** 497 (Nov) 1943.

18 Tolan, T L. Report on Two Cases of Carcinoma of Sphenoid and Ethmoids, *Ann Otol, Rhin & Laryng* **48** 1067 (Dec) 1939.

the forehead and the cornea, vasomotor disturbances, and impairment of vision, which in many cases results in blindness. Pain is fairly constant. It is localized behind the eyeball and radiates to the top of the head, to the forehead and to the temples. The pain usually subsides when the ophthalmoplegia is at its height.

Other signs are diplopia, ophthalmoplegia of varying degree, including ptosis, loss of accommodation, and an enlarged, fixed pupil. There may be only slight changes in the fundus, but involvement of the optic nerve occurs, with atrophy of the nerve, late in the condition. Exophthalmos is not a typical finding and is only slight when present. The syndrome may be bilateral but usually affects only one eye at a time. Months or years may elapse before the other eye becomes involved.

An interesting case of the complete syndrome is reported which was due to a malignant process extending laterally from the sphenoidal sinus to involve the structures which leave the adjacent cavernous sinus to enter the sphenoidal fissure and the optic canal.

REPORT OF CASE

Mrs. Y. S., a Jewish woman aged 58, was referred by Dr. Edward Rubin and was admitted to the medical ward service of Dr. A. I. Rubinstein of the Mount Sinai Hospital, Philadelphia, on Nov. 26, 1945. The chief complaint was headache, which had become very severe in the last two months, and severe, persistent epistaxis of about one week's duration.

Past History—The past medical history revealed moderate hypertension of ten years' duration, with angina pectoris on moderate effort for the past three years. The patient had had moderate menopausal symptoms since 1940, when her menses ceased. She had 3 children, who were living and well. She did not recall any serious illnesses except for typhoid in 1905 and influenza in 1918.

She had had mild, infrequent headaches since early adult life. In 1941 these headaches, although still infrequent, became more severe and were described as shooting pains in her head associated with dizziness. It was thought that these headaches were due to cerebral arteriosclerosis associated with moderate menopausal symptoms. In July 1945 the headaches became more frequent and once again were "shooting" in character but lasted only a few seconds. In September 1945 the sharp, shooting headaches recurred daily. In November 1945 they were almost constant, with no relief from analgesics. The patient was now confined to bed. She complained of a burning sensation on the scalp associated with the head pains. The pain radiated over the right temple, and the right side of the forehead and over both eyebrows, being more severe over the right one, and was also localized in her right ear. Her nose also became stuffy, especially on the right side, due to a boggy, pale, allergic-appearing nasal mucosa. At this time a rhinologic examination revealed no other abnormalities. On November 16, ten days before admission, she had a severe nosebleed from the right side. This persisted intermittently until she was admitted to the hospital. Two days prior to admission the blood pressure was 200 systolic and 100 diastolic, and general physical examination revealed otherwise an essentially normal state. The eyes at this time showed no visible abnormalities except for slightly distended retinal veins on ophthalmoscopic examination. The head pains now became knifelike and excruciat-

ing, they still radiated to the forehead, the right temple and both eyebrows, being most severe over the right eyebrow and the right eye

Physical Examination—On admission, on November 26, her height was 5 feet and her weight 125 pounds (56.7 Kg). Her normal weight was 130 pounds (59 Kg). The blood pressure was 160 systolic and 90 diastolic, the pulse rate was 90 and the rhythm regular, the temperature was 98.6 F, and the respiratory rate, 21 per minute. Soon after admission she again bled intermittently from the right nostril. No definite bleeding points could be seen in the nose. The physical examination otherwise showed nothing abnormal except for a few suspicious-looking teeth. The electrocardiogram was within normal limits. The eyegrounds were normal except for arterial contraction and a slight arteriovenous crossing phenomenon. No other ocular abnormalities were noted. On the morning of November 28 the epistaxis became profuse and remained so for about eighteen hours, when her nose was firmly packed. She had lost a great deal of blood, however, and the hemoglobin concentration dropped from 96 to 68 per cent.

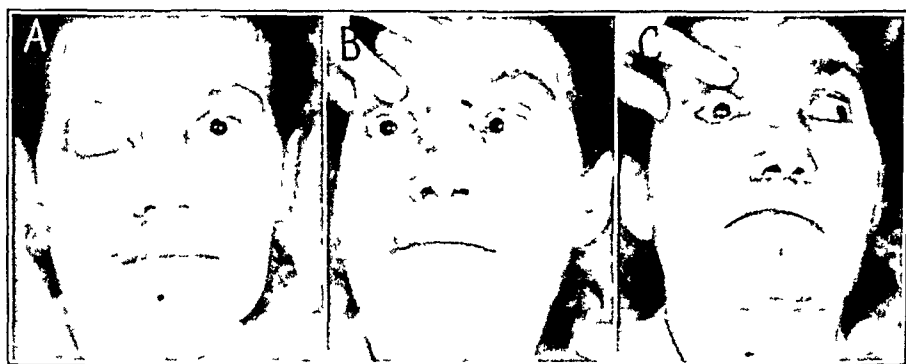


Fig 1—*A*, patient looking straight ahead, showing complete ptosis of the right upper eyelid, *B*, patient looking to the right, showing fixed position of the right eye, *C*, patient looking to the left, showing fixed position of the right eye.

Ophthalmic Examinations—*Right Eye* On November 30, four days after admission, she suddenly lost the vision in the right eye. On the following day a partial ptosis of the right upper eyelid was noted. The right pupil was dilated to about 6 mm in diameter and failed to react to light. At this time ophthalmoscopic examination revealed no cause for the loss of vision. Other than distention of the central veins and narrow, tortuous arteries, the fundus was essentially normal. Three days later the ptosis of the right upper eyelid was complete and the pupil was widely dilated and fixed. There was now no rotation of the right eye upward, inward or outward, and there was impaired downward rotation.

Within the next two days (December 5) the right eye became completely immobile and fixed in the midposition, with a dilated fixed pupil. Corneal sensitivity was absent. The ophthalmoplegia was now complete—six days after her vision failed. There was no exophthalmos.

Left Eye The rotations of the left eye were full in all directions, and the findings on external examination were normal. On ophthalmoscopic examination, the media was clear, the optic disk round and the margins well outlined, with normal color. The retinal vessels showed the changes of hypertension and arteriosclerosis, but no other pathologic condition was seen.

Roentgenographic Examination—A roentgenogram of the skull was reported to show an essentially normal condition. At this time roentgenographic examination of the sinuses showed that the frontal sinuses were not developed, the right ethmoid cells were partially clouded, the right antrum was uniformly clouded, and the sphenoidal sinus was clear in a lateral view. The left ethmoid cells and the left antrum were clear. Special roentgenograms of the sphenoidal sinus were not taken at this time. A roentgenogram of the orbits revealed nothing abnormal.

On December 10, the hearing became impaired, and pus was found in the right middle meatus, with bilateral acute otitis media. The latter was thought to be the cause of the deafness. Treatment with sulfadiazine, 1 Gm every four hours, and penicillin, 50,000 units every three hours, was started. In two days the temperature fell to normal and the otitis media improved, but the deafness continued. The next day, December 9, the temperature for the first time rose to 101 F (rectal). The nasal packing was removed, with no bleeding occurring. A direct nasal pharyngoscopic examination on December 19 visualized the entire nasopharynx. No neoplasm was seen. Some mucoid secretion was present in each eustachian orifice. On December 22 a rise in temperature, due to bilateral basal pneumonitis, occurred. The patient had received about 50 Gm of sulfadiazine and about 5,000,000 units of penicillin.

On December 24 the patient became worse. In addition to complete ophthalmoplegia on the right side, she now presented considerable edema and puffiness of the upper and lower right eyelids, extending down over the right side of the face. There was a moderate amount of chemosis of the bulbar conjunctiva but no exophthalmos. The right fundus now showed changes for the first time. There was edema about the nerve head, extending slightly beyond the margin of the disk, and several small, superficial hemorrhages were seen lying close to the inferior temporal artery. There were also several small, superficial hemorrhages in the upper temporal region. The retinal veins were distended, but no other pathologic change was seen. The left eye was essentially normal.

In consultation with the rhinologist, Dr Benjamin Shuster, and the neurosurgeon, Dr Henry Shenkin, an exploration of the right orbit was decided on, after insertion of an exploratory needle had proved unsuccessful.

On December 27, with local anesthesia, the right orbit was explored from the medial aspect. An incision was made along the right side of the nose at its root and extended under the right eyebrow for a distance of about 2.5 cm. The incision was made down to the periosteum. The medial, the inferior, the superior and part of the lateral wall of the orbit were explored, without encountering any abnormality. The periorbital fat was incised on the medial aspect, and no masses could be palpated. The wound was dressed with sulfanilamide powder, iodoform gauze packing and two sutures.

A review of the roentgenograms was made at this time, with a special view to better visualization of the sphenoidal sinuses. This revealed loss of outline of the posterior wall of both sphenoidal sinuses with generalized haziness. This was interpreted to indicate a destructive lesion involving the sphenoidal sinuses.

Operation—The patient was then returned to the operating room, and, with the use of local anesthesia, an extensive sphenoidectomy, ethmoidectomy and antrotomy through the nasal approach was performed on the right side by Dr Benjamin Shuster. The posterior wall and part of the anterior wall of the sphenoidal sinus were absent, probably because of erosion by malignant tissue.

What appeared to be normal middle turbinate was removed and found to show suspicious evidence of a malignant growth. There was considerable bleeding during the entire operation. Most of the ethmoid cells were removed. None were bony, but they contained degenerated soft tissue. The interior of the sphenoidal sinus could be visualized. It contained similar soft, pinkish gray, slightly friable tissue. Much of this tissue was removed. The right antrum was also entered. Some pus was observed here, with a considerable amount of similar neoplastic-appearing tissue, much of which was removed through the middle meatus. The wound was packed with iodoform gauze.

Pathologic Report—All the material removed consisted of a small amount of pinkish gray, slightly friable tissue from the sphenoidal sinus and a large amount of pinkish gray, soft tissue, with a few pieces containing small cores of bone.

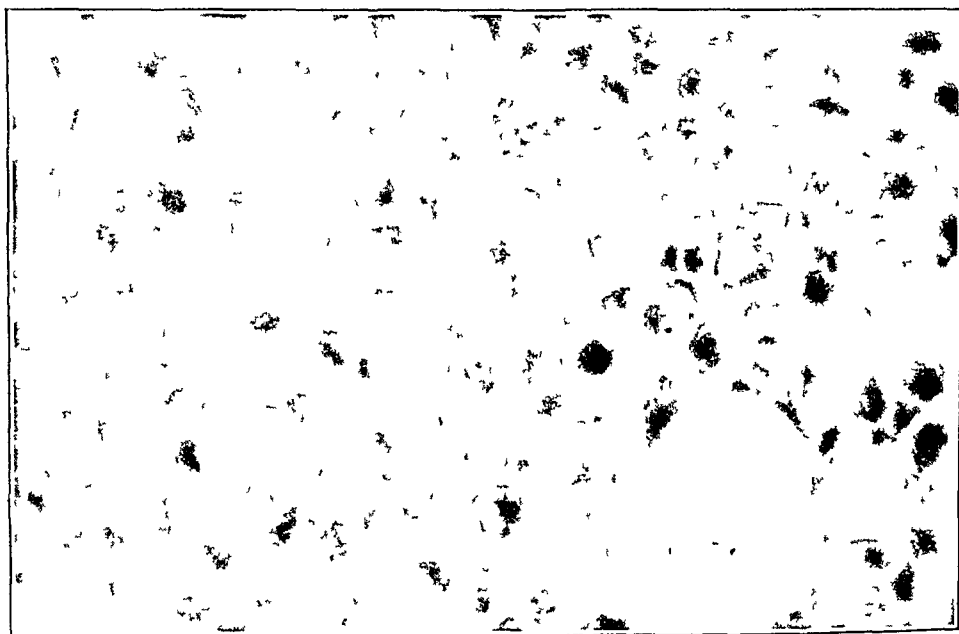


Fig 2—Microscopic section of the carcimatous tissue removed from the sphenoidal sinus

tissue, from the ethmoid cells, the antrum and the nasal mucosa. Histologic examination by the pathologist, Dr David R Meranze, showed that the tissue from the sphenoidal sinus and that removed from the ethmoid cells, the antrum and the nasal mucosa were similar. It was all reported as definitely malignant, resembling carcinoma. Clumps of malignant cells were seen within lymphatic and vascular channels. Necrosis, hemorrhage and suppuration were present. The pathologic diagnosis was "necrotizing, hemorrhagic, suppurative carcinoma invading the lymphatics and vascular channels, probably primary in one of the nasal sinuses."

Postoperative Course—The nosebleed was excessive after the operation but gradually subsided. The head pains also gradually subsided, with a slight residual pain over the right eye and the right temple. The deafness, although slightly improved, was still present. The otitis media cleared up.

Intensive roentgen therapy was started after operation. This was followed by improvement in the general physical condition and morale of the patient. The right upper eyelid continued to be moderately swollen, and ptosis was complete. There were pronounced chemosis and congestion of the bulbar conjunctiva, and the eye was still fixed in midposition. The pupil was dilated and fixed.

Ophthalmoscopic examination of the right eye on January 14, sixteen days after operation, revealed the presence of considerable edema on and about the right optic disk, with several fair-sized hemorrhages overlying the disk. There was also an increased number of smaller hemorrhages outside the disk. The left eye was normal.

Treatment—Treatment consisted of transfusion of 500 cc of whole blood in each of four transfusions and administration of 8,880,000 units of penicillin in twenty-six days, between Dec 10, 1945 and Jan 5, 1946, 60 Gm of sulfadiazine in fifteen days, between December 10 and December 25, and large doses of vitamins and iron by mouth. From a medical viewpoint it is interesting to note that bilateral basal pneumonitis developed while the patient was receiving sulfadiazine and penicillin, 50 Gm and 5,000,000 units, respectively. The pneumonitis was most likely of virus origin. At the time of this report, the patient is still receiving roentgen therapy, with little change in the ocular or general condition. It is expected that a further report of this case may be made some time in the near future.

Laboratory Studies—Urinalyses showed essentially a normal state except for a trace of albumin. The hemoglobin fell from 96 to 68 per cent and gradually rose to 76 per cent after four transfusions of whole blood of 500 cc each. The red cell count was 3,490,000. The white cell count ranged from 7,400, on admission, to 13,140, on January 11. The differential count showed a slight increase in the polymorphonuclear leukocytes. On admission there were 64 per cent segmented polymorphonuclear cells, 2 per cent nonsegmented forms and 34 per cent lymphocytes, and on January 11, 73 per cent segmented forms, 9 per cent nonsegmented forms, 15 per cent lymphocytes and 3 per cent monocytes. The platelet count was 290,000 on December 6, with a coagulation time of five and a half minutes and a bleeding time of two minutes. The total serum protein and the albumin-globulin ratio were normal. Renal function was normal. The prothrombin time was 65 per cent on December 6. The sedimentation rate was normal.

A spinal puncture, performed December 4, with the patient in sitting position, revealed an increased pressure of 294 mm of water, with clear fluid and essentially normal cellular and chemical findings. The serologic reactions were negative, the colloidal gold was normal, and smears and culture revealed no pathogens. The serologic reactions of the blood (Kolmer and Kline) were negative. The blood sugar was moderately elevated, reaching 180 mg per hundred cubic centimeters. It was later maintained at a level of about 145 mg per hundred cubic centimeters.

SUMMARY AND CONCLUSIONS

A case of carcinoma primary in the sphenoidal sinus occurred in a woman aged 58 who presented all the ocular signs and symptoms of involvement of the structures passing through the sphenoidal fissure and the optic canal without destruction of the inner walls of the orbit. The right ethmoid cells and right maxillary sinus were also involved by the malignant process.

Epistaxis was unusually severe and prominent, although this symptom has rarely been mentioned in any of the other cases reported. Together with the headache, it was an initial symptom.

Severe, sharp, knifelike pains radiated over the forehead, the right temple and both eyebrows, being more severe over the right side. There was also a burning sensation of the scalp.

The ophthalmoplegia came on rather quickly. It was complete within six days after appearance of the first ocular signs. In most of the cases in which the syndrome is due to a malignant growth, the symptoms have a much slower onset and are more gradual in their progress.

In this case the carcinoma must be seriously considered as primary in the sphenoidal sinus. As previously stated, primary malignant growths in the sphenoidal sinus are rare, only about 42 cases having been reported. It is difficult to state definitely that a malignant growth arises primarily in the sphenoidal sinus, because in most cases operation is done too late. This was also true in the present case, but the following factors make me feel that the sphenoidal sinus must be considered as the primary source: the clinical history of severe headache and pain over the forehead and eyes, the fact that a careful examination of the nose, throat and ears just before hospitalization revealed essentially nothing abnormal, the absence of frontal sinuses, the bilateral involvement of the sphenoidal sinuses roentgenologically, while the ethmoid cells and antrum were involved only on the right side, all would indicate with considerable certainty that the carcinoma arose in the sphenoidal sinus. It eroded the walls of the sinus and most likely invaded the region of the right cavernous sinus with involvement of all the structures.

If the malignant growth originated in the maxillary sinus, it would have invaded the orbit as well as the ethmoid cells. If it had originated in the ethmoid cells, it would probably have invaded the nose and also the orbit by the time it became extensive enough to involve both sphenoid sinuses and the right antrum. It is therefore reasonable to assume that the sphenoidal sinus was the original site of involvement.

The infrequency of reported cases of this syndrome in the American literature, and particularly in the ophthalmic literature, makes this case worthy of presentation.

Most of the cases recorded in the past were incomplete in their manifestations and were described under various names, most common of which was the "orbital apex-sphenoid fissure syndrome."

In my opinion, only cases in which the ophthalmoplegia is complete should be included in this group. Furthermore, the name of the syndrome should be more specific for and descriptive of the symptom com-

plex Since it results from a morbid process involving the part of the sphenoid bone which includes the sphenoidal fissure and optic canal with the structures they contain, the syndrome could be more accurately designated as the sphenoidal fissure-optic canal syndrome with complete ophthalmoplegia The condition should be suspected early, however, in cases of paralysis of any of the nerves involved and accompanied with the symptoms described Blindness might be avoided in some cases in which the condition is recognized before the optic nerve becomes involved by the process

NOTE—Since this case was reported, I have had the opportunity to study 2 additional cases in which the cause was the same These will probably be included in a future report

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TREATMENT OF LATE POSTOPERATIVE INTRAOCULAR INFECTIONS WITH INTRAOCULAR INJECTION OF PENICILLIN

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AND

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A SIGNIFICANT literature has been created on the experimental treatment of intraocular infections with penicillin. The various routes of administration and the concentration obtained in the various tissues of the eye have been studied in several laboratories, notably by von Sallmann and by Leopold and their co-workers. However, there have been but few reports on the effect of intraocular injection of penicillin in man.

The following 2 cases are presented because extracapsular cataract extraction was followed by late intraocular infection and was treated with intraocular injections of penicillin.

REPORT OF CASES

CASE 1—D. W. N., aged 63, was readmitted to the Veterans Administration Hospital on Aug. 28, 1945 for extraction of cataract in the right eye. He had had an intracapsular cataract extraction from the left eye in May 1945, with an uneventful postoperative course. He was found to have no foci of infection. He received zephiran chloride (1:3,000), 1 drop three times a day, in the right eye for twenty-four hours prior to operation. The attempt to perform an intracapsular cataract extraction was unsuccessful, and the capsule of the lens was torn. A broad iridectomy was done, and extracapsular cataract extraction was completed. The anterior chamber was irrigated with sterile isotonic solution of sodium chloride, and the wound was closed by tying the Stallard suture. The following day the anterior chamber was formed. The patient received typhoid-paratyphoid A and B vaccine, 10,000,000 organisms, intravenously as a prophylactic measure because there had been considerable manipulation in the anterior chamber during the operation. On the seventh postoperative day the anterior chamber appeared cloudy and within thirty-six hours was filled with a dense creamy fibrinous exudate. He received 50,000 units of penicillin intramuscularly every three hours and typhoid-paratyphoid A and B vaccine, 20,000,000 units twice a week intravenously. Two days later the corneoscleral wound was gaping. A penicillin eye bath (2,500 units per cubic centimeter) with 2 drops of zephiran chloride (1:3,000 dilution) as a wetting agent was used in an eye cup for ten minutes every hour. He also

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received penicillin ointment (2,500 units per cubic centimeter) locally at bedtime. Intracorneal paracentesis was done the next day, and cultures of the fluid of the anterior chamber yielded *Staphylococcus aureus*. Through the paracentesis wound 500 units of penicillin in 0.2 cc of distilled water was injected into the anterior chamber. This was repeated once daily, in addition to the penicillin eye baths and intramuscular injections. He received sulfadiazine orally for seven days, penicillin was given intramuscularly and was injected into the anterior chamber for fourteen days. The exudate absorbed slowly. A conjunctival flap was made eighteen days after the onset of infection. Superficial and deep corneal vascularization appeared but responded well to roentgen therapy and riboflavin, 30 mg daily. Three months after operation he had a dense corneal opacity with organized exudate in the anterior chamber, but minimal vascularization. Vision was limited to light perception and faulty projection. The tension was normal.

CASE 2—W. A. R., aged 46, was admitted to the Veterans Administration Hospital on Sept. 28, 1945 for extraction of traumatic cataract. On Oct. 8, 1945, he had had an extracapsular cataract extraction. He received typhoid-paratyphoid A and B vaccine intravenously every two days from the second to the ninth day to hasten absorption of the lens cortex. On the eleventh postoperative day he had a painful, reddened eye with a cloudy anterior chamber, a muddy iris and a small hypopyon. He was given penicillin, 100,000 units intramuscularly every three hours, sulfadiazine, 15 grains (0.975 Gm) orally every four hours, and atropine and hot compresses locally. Paracentesis was done, and the fluid of the anterior chamber showed *Staph aureus* on culture. The hypopyon did not reappear, but two days later edema of the upper lid became apparent. There was no improvement, and on the twenty-fourth postoperative day (thirteen days after the appearance of endophthalmitis) an intravitreal injection of 500 units of penicillin dissolved in 0.2 cc of distilled water was given through an opening in the sclera 12 mm from the limbus. Postoperatively, treatment with penicillin, typhoid-paratyphoid A and B vaccine and sulfadiazine was continued. The next day scleral injection and cloudiness of the anterior chamber diminished. Thirteen days after the intravitreal injection of penicillin all therapy except for mydriatics was discontinued. Six weeks later he was found to have light perception with faulty projection. There was a faint aqueous flare. The iris was displaced slightly upward and temporally, with the pupil measuring 1 mm in diameter and the iris adherent to the anterior limiting membrane of the vitreous. The eye was soft but not phthisical.

COMMENT

High concentrations of penicillin can be produced in the anterior chamber by several means. Von Sallmann and Meyer¹ produced high levels in the normal rabbit eye by the corneal bath and iontophoresis. Struble and Bellows² reported that the corneal bath gave higher concentrations of penicillin in the aqueous than subconjunctival injection. The studies of Leopold and LaMotte³ indicated that repeated local

1 von Sallmann, L., and Meyer, K. Penetration of Penicillin into the Eye, *Arch Ophth* **31**:1 (Jan) 1944.

2 Struble, G. C., and Bellows, J. G. Studies on the Distribution of Penicillin in the Eye, *J. A. M. A.* **125**: 685 (July 8) 1944.

3 Leopold, I. H., and LaMotte, W. O., Jr. Penetration of Penicillin in Rabbit Eyes with Normal, Inflamed and Abraded Corneas, *Arch Ophth* **33**: 1 (Jan) 1945.

application of penicillin has no deleterious effect on regeneration of corneal epithelium. Dunnington and von Sallmann⁴ reported that repeated injections produced lenticular opacities and synechias, they recommended administration by iontophoresis and by subconjunctival injection. However, reports from Alpert⁵ and the Ninth Evacuation Hospital⁶ do not corroborate their findings in man.

In cases of severe infection of the vitreous there is no question that the only means of obtaining adequate concentration of penicillin is by direct intravitreal injection. Leopold⁷ reported that penicillin given systemically does not produce an adequate concentration in the vitreous for therapeutic purposes. Von Sallmann, Meyer and Di Grandi⁸ advised the use of a fine needle and the injection of penicillin into the central portion of the vitreous to minimize the possibility of producing traumatic cataract or retinal detachment. Von Sallmann⁹ stated that a twelve hour interval between infection and administration of penicillin is the limit for satisfactory treatment of experimental exogenous infections of the vitreous. This time limit can be extended to similar conditions of the human eye, but encouraging results can be obtained even after signs of severe endophthalmitis have become apparent clinically.

Of the 2 patients whose cases are reported here, the first had a severe fulminating infection of the anterior chamber. He received 500 units of penicillin intraocularly daily for two weeks. One cannot state how much of the residual scarring was due to the infection and how much was caused by the penicillin. However, there is no question that the infectious process was responsible for most of the damage. The second patient was given 800,000 units of penicillin and 90 grains (5.85 Gm.) of sulfadiazine systemically daily for thirteen days, with no improvement. As a last resort, penicillin was injected into the vitreous, with a dramatic response.

As a rule, eyes with postoperative infections as severe as that in the 2 cases reported here continue to become worse and finally require evisceration. In fact, evisceration was considered in both cases prior

4 Dunnington, J. H., and von Sallmann, L. Penicillin Therapy in Ophthalmology, *Arch Ophth* **32** 353 (Nov) 1944

5 Alpert, D. R. Intraocular Injection of Penicillin in a Case of Ring Abscess of the Cornea, *Am J Ophth* **28** 64 (Jan) 1945

6 Notes on Penicillin in Ocular Infections, *M. Bull. Mediterranean Theat Op* **2** 167 (Dec) 1944

7 Leopold, I. H. Intravitreal Penetration of Penicillin and Penicillin Therapy of Infections of the Vitreous, *Arch Ophth* **33** 211 (March) 1945

8 von Sallmann, L., Meyer, K., and Di Grandi, J. Experimental Study on Penicillin Treatment of Exogenous Infection of Vitreous, *Arch Ophth* **32** 179 (Sept.) 1944

9 von Sallmann, L. Penicillin Therapy of Infections of the Vitreous, *Arch Ophth* **33** 455 (June) 1945

to injection of penicillin into the globe. Perhaps, if we had used intraocular injections earlier in the course, our results would have been better. The concentration of penicillin used intraocularly was the one found safe in animal studies. It is possible that stronger concentrations of penicillin may be tolerated just as well by man and give better results. As it is, we can only say that both eyes tolerated the injections of penicillin and went on to rather rapid quiescence soon after the injections were given.

CONCLUSIONS

1 The intraocular injection of penicillin for late postoperative infections is well tolerated by man.

2 The eye which becomes infected postoperatively may be saved from evisceration by early injection of penicillin directly into the involved area.

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PSEUDO-GRAEFE PHENOMENON

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Translated from the Portuguese by Eugene Ressencourt
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I DO NOT know whether it was merely a matter of luck that I was unable to discover, among the pages of such Brazilian magazines of ophthalmology as I could lay my hands on, any observation on the pseudo-Graefe phenomenon (Bielschowsky) or to learn whether such an anomaly, also called "Fuchs's sign," and even the "pseudo-Graefe syndrome," really constitutes a rarity among associated movements of the eyelids. This is the curious phenomenon which I shall discuss in this paper and with which I was acquainted only through a few cases reported in foreign technical books and journals.

CASE UNDER MY SUPERVISION

On Jan 23, 1944 Miss I G R, a Brazilian white woman, aged 20, suffered an accident (a fall from a horse) and shortly thereafter went into coma, which lasted three days. Flaccid hemiplegia of the left side of the body developed, and she remained in a state of unconsciousness for twenty-five days. At this time several roentgenograms were made but they showed no sign of a fracture. Examination of the spinal fluid revealed red blood cells. After the twenty-fifth day a gradual improvement of the patient's condition was noted.

On Aug 16, 1944, when she was examined by my distinguished colleague, the neurologist Dr Cortes de Barros, the patient showed only the ocular symptoms hereafter described, together with slight adiadokokinetik disturbances, noticeable only in rapid movements of the hand. The next day I examined the patient and found that the ocular abnormality was total paralysis of the left oculomotor nerve, with partial functional recovery of the internal rectus muscle and barely appreciable functional recovery of the levator muscle (figure A). I determined,

This paper was read, with the patient present, at a meeting of the Brazilian Ophthalmological Society in Rio de Janeiro on May 18, 1945, it was then commented on by Dr Paulo Filho, who called attention to the possibility that the patient's ptosis might be only a defense attitude against double vision. After thanking Dr Paulo Filho for his comment, I replied that such a hypothesis was not acceptable, for the following reasons: (1) The patient did not complain of double vision when both eyes were open, even with a red glass held before one eye, (2) it was customary for her to keep both eyes open, for, being a student, she spent hours in reading, with the right eye directed downward and the left eyelid in a retracted position, and this without the slightest inconvenience.

further, that with correction of the slight hypermetropia visual acuity of 20/20 was obtained in each eye. Everything else was normal, including the fundus oculi and the visual field for white and other colors. I attributed the paralysis to a lesion in the trunk of the left oculomotor nerve, and I advised the patient to continue with the treatment recommended by Dr. Cortes de Barros. Some days later she reported to me that she was feeling better, for she had already succeeded in moving the fallen eyelid. Examining her again, I observed that indeed the upper lid of the left eye rose, but only when the patient directed her gaze downward or to the right (figure, *B* and *C*). Not many days had passed before the patient came to me to demonstrate that also when she directed her gaze upward the lid of the left eye retracted (figure, *D*). In the effort of directing the gaze upward, as well as of directing it downward, especially in



A shows the patient's present habitual ocular condition, *B* shows the patient looking downward and the resulting retraction of the upper left eyelid, *C*, the patient looking to the right (and slightly downward) and the resulting retraction of the upper left eyelid, *D*, the patient looking upward and the resulting retraction of the upper left eyelid, *E*, the patient with the right eye closed and directed downward and to the right beneath the closed lid, with retraction of the upper left eyelid, and, *F*, the patient looking to the left, with no retraction of the upper left eyelid.

the case of the latter, the left eye moved slightly inward concomitantly with the retraction of its upper lid. A week later she noticed that with the right eye closed she could raise the fallen lid (figure, *E*). In looking to the left, the left eye remained shut (figure, *F*). These symptoms correspond exactly with those reported under the name of "Fuchs's sign" (or even under the designation "pseudo-Graefe syndrome" or "pseudo-Graefe phenomenon," through the similarity to retraction of the upper lid during downward gaze in cases of exophthalmic goiter).

ABSTRACT OF CASES FROM PUBLISHED MATERIAL

Bielschowsky,¹ of Breslau, Germany, has published 5 cases of the "pseudo-Graefe phenomenon" I shall summarize them as follows

CASE 1—A man of 30 suffered paralysis of the right oculomotor nerve through a fracture of the base of the skull. Three months later examination revealed, as a residual of the paralysis, only moderate dilatation of the right pupil, a very slow reaction to light, an almost normal reaction of the pupil in convergence and pupillary slight paresis of the superior rectus muscle. The eyes were parallel in the primary position, and the upper lids were raised equally. In looking downward and to the right, both eyelids followed the eyes normally, whereas in looking downward and to the left the upper lid of the right eye retracted and the pupil of this eye narrowed in such a way that the dissimilarity of the pupils disappeared.

CASE 2—A woman of 39, six months after sustaining a fracture of the base of the skull which produced total paralysis of the third and seventh nerves, presented the following conditions: absence of ptosis in the primary position of the eyes, normal synergy of the eyes and upper lids when looking down and to the right and considerable retraction of the right upper lid when looking down and to the left. At the same time, the dilated pupil of the right eye contracted, it did not respond to light, and its reaction in convergence was imperfect.

CASE 3—A woman of 28 had total paralysis of the right oculomotor nerve, the origin of which had not been determined. Five months later there was also retraction of the right upper eyelid in looking downward and to the left, and the pupil was contracted, as in the 2 previous cases.

CASE 4—A student had total paralysis of the left oculomotor nerve as the result of a fracture of the base of the skull. The patient was under the author's (Bielschowsky's) observation for over three years. Only fifteen months after the fracture had occurred was the first change observed. Then it was seen that a few folds appeared in the upper lid, which had been completely relaxed until then, and that the patient when looking directly to the front was able, with the greatest effort, to open the lid 3 mm. When he looked to the left, the eyelid was completely relaxed, and he could not raise it at all, but when he made a great effort to look downward, the lid raised itself a few millimeters automatically. This retraction was greater when the right eye was directed upward. When an effort was made to look to the right, a maximal retraction of the left upper lid was observed.

CASE 5—A woman had syphilis of the basal portion of the brain, which resulted in atrophy of the left optic nerve, paralysis of the left fifth nerve and total left ophthalmoplegia. The left eye could not be moved. The left upper eyelid could not be raised with any amount of effort, it remained relaxed even when the patient looked upward. But when she looked to the right, the lid was automatically raised a little, and when she looked downward, it was raised still more, as the right upper lid, which was normal, reached its lowest position.

In commenting on these cases, Bielschowsky asserted that Fuchs explained the phenomenon as follows. In consequence of a lesion of the nucleus of the third nerve, or atrophy thereof through retrograde

1 Bielschowsky, A. Lectures on Motor Anomalies of the Eyes. Paralysis of Individual Eye Muscles, *Arch Ophth* 13 33-35 (Jan) 1935

degeneration, the nervous stimulation received by a part of the nucleus spread to the surrounding portions in such a way that they also were stimulated and involuntary movements occurred. Bielschowsky took exception to this theory with respect to those patients who presented retraction of the upper eyelid despite the fact that all the external ocular muscles had completely lost their function, the levator of the eyelid reacting only automatically to impulses sent to specific muscles, principally the depressors, which have no physiologic connections with it. Moreover, in practically all his patients who presented this phenomenon the lesion producing paralysis of the oculomotor nerve was localized at the base of the skull. He went on to say that he could not conceive of a complete retrograde degeneration of the nucleus, such as Fuchs pictured, in which only the innervating nucleus of the levator muscle would not be affected and, not being able to respond voluntarily to stimulation, would be sensitive only to impulses sent to other, atrophic, parts of the nucleus of the third nerve. Bielschowsky expressed his belief that the pseudo-Graefe phenomenon could be explained as follows. Suppose that the continuity of the oculomotor nerve is interrupted by a tumor or by trauma and that in the course of healing some of the nerve fibers from the central part of its trunk do not connect with their respective original sheaths in the peripheral part and wander off to alien muscles. For example, fibers belonging to the internal rectus muscle might make connections not with this muscle but with the levator muscle of the eyelid, with the result that impulses to adduction of the eye cause an elevation of the upper lid, even though it cannot be raised by an effort of direct innervation, inasmuch as the fibers from the nucleus for the levator muscle have wandered off. In a few cases some of the nerve fibers destined for the levator muscle reach this muscle along with fibers of other origin, and thus, while there is no ptosis, there is an abnormal retraction of the upper eyelid when impulses are sent to other muscles. It seems, as Bielschowsky suggested, that the nerve fibers, when regenerating, prefer to grow in certain directions, which lead them to the wrong sheaths, and thus in most cases the impulse to look downward and inward causes the strongest retraction of the upper lid. It is interesting to note that in 3 of Bielschowsky's 5 cases the paralyzed or paretic pupil contracted when the gaze took directions in which the upper lid rose.

Especially interesting is a case which Bender² reported and presented at a meeting of the New York Neurological Society in which the

2 Bender, M. B. (a) The Nerve Supply to the Orbicularis Muscle and the Physiology of Movements of the Upper Eyelid, with Particular Reference to the Pseudo-Graefe Phenomenon, *Arch. Ophth.* **15** 21-30 (Jan.) 1936, (b) Abnormal Associated Movements of the Eyelid (Pseudo-Graefe Sign), *Arch. Neurol. & Psychiat.* **35** 403 (Feb.) 1936.

phenomenon appeared after removal of a parasellar osteochondroma. This case was also reported by Levitt.³ In a word, examination revealed the following conditions in the left eye: paralysis of the superior and inferior rectus muscles and the oblique muscles and slight paresis of the external rectus muscle, semidilatation and immobility of the pupil, and absence of ptosis, although the palpebral fissure was slightly smaller than that of the right eye. The patient was able to close either eye with the same amount of effort, but when he looked downward the left upper eyelid remained elevated and the eye moved slightly inward. Moreover, when the patient tried to look downward with the eyes closed, the upper left eyelid suddenly retracted and assumed the same abnormal position as when the patient looked downward with his eyes open. Concerning this last condition, Bender said:^{2a}

with eyes initially closed, an upper lid snaps upward when an attempt is made to look down. The latter abnormality, hitherto undescribed, is probably another form of the pseudo-Graefe phenomenon.

Basing his contention on Mendel's statement, which he cited, that the orbicular muscle is innervated not only by the facial nerve but also by nerve fibers that have their origin in the posterior portion of the nucleus of the third cranial nerve and pass along with fibers destined for the levator of the eyelid, and also taking cognizance of the fact the automatic and reflex winking movements may occur through contraction, synchronous or separate, of the parts of the orbicular muscle,⁴ Bender suggested that in cases of neuropathy of the facial nerve (Bell's paralysis), as in the normal eye, the involuntary movement of lowering the upper eyelid in looking downward is due to contraction of a part of the orbicular muscle rather than to relaxation of the levator, the contraction following the nerve impulse to the orbicular muscle via fibers that would run in the branch of the oculomotor nerve which innervates the levator muscle. Bender expressed the opinion that, according to this theory, the absence of involuntary action of the upper eyelid in looking downward (the pseudo-Graefe phenomenon) is due to an increase in the tonus of the levator muscle. He supported the last statement with the following facts: (a) In the fixed downward glance, the affected eyelid being forcibly drawn down also, relaxation of the force applied is followed by sudden raising of the same eyelid, (b) the eyelid resists when it is being drawn

3 Levitt, J. M. Unilateral Ophthalmoplegia Totalis, Parasellar Osteochondroma, *Arch Ophth* **12** 877-886 (Dec.) 1934.

4 Duke-Elder, W. S. Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1933, vol. 1, p. 634, cited by Bender.^{2a}

downward, and (c) when the patient looks downward with the eyes initially closed, the affected eyelid suddenly retracts. Bender concluded that in the pseudo-Graefe phenomenon the tonicity of the levator muscle, when the eyes are directed downward, is greater than that of the orbicular muscle. He cited as well the theory advanced by Fuchs, who, he stated, described the phenomenon in 1893, Gowers, before him, having observed 2 cases in 1879, and the theory proposed by Bielschowsky, which he said was based on Lipschitz' explanation of the frequent occurrence of abnormal movements of the facial muscles in patients during recovery from Bell's paralysis. A further statement by Bender follows ^{2a}

It has been shown by Ramon y Cajal that in the repair of a damaged nerve the regenerating nerve fibers reach the peripheral stump in great disorder. The greatest number of sheaths, instead of receiving the outgrowths of the corresponding axons, are invaded by sprouts derived from axons in other regions of the central stump. Under such conditions, an impulse originally directed to one muscle will deviate to another and produce a contraction in the muscle for which it was not intended. Thus, in patients manifesting the pseudo-Graefe phenomenon, it is probable that the regenerated fibers of the third cranial nerve trunk innervate chiefly the levator palpebral and internal rectus. For example, axons which were supposed to have reentered the nerve sheath of the nerve bundle supplying the inferior rectus muscle have instead regenerated into the sheaths of nerves supplying the levator and internal rectus. Consequently, an impulse meant for the inferior rectus will be propagated to the levator and internal rectus, producing a light contraction in these muscles. At the same time, the relaxation of the levator, which is supposed to be present when the eyelid moves downward, does not take place. It is also probable that fibers from the other bundles of the third cranial nerve enter the "regenerated pathways," producing the slight motion of the internal rectus on upward gaze.

Bender also referred to a case of Halpern's, that of a patient with paralysis limited to the levator muscle, resulting from a gunshot wound in the head in which the bullet lodged in the base of the skull on the right side. For three months there was no sign of any lesion except for complete ptosis of the right eyelid. Then the ptosis disappeared and the pseudo-Graefe phenomenon appeared. Downward movements of the eye were perfect. The eyelid retracted on his looking downward and inward but only infrequently when he was looking inward. Bender expressed the opinion that this case demonstrated also the possibility that the pseudo-Graefe phenomenon resulted from a lesion confined to the levator part of the oculomotor nerve and that, granting to be true the theory of innervation of the orbicular muscle by fibers of the oculomotor nerve accompanying fibers to the levator muscle, the following inference might be made. By virtue of the defective regeneration of the nerve fibers, the impulse directed to the orbicular muscle for

the involuntary movement executed by the upper eyelid in looking downward would be switched to the levator muscle and give it, in such a position, a tonicity greater than that of the orbicular muscle, a condition which would make impossible the normal associated movement. Bender, therefore, claimed that the pseudo-Graefe phenomenon results from tonic innervation of the levator muscle in the course of defective regeneration of the nerve fibers, nerve impulses being switched to it which were destined for the orbicular muscle or for other muscles.

Gifford,⁵ in an interesting article on a subject correlated with the matter under discussion, stated that Thurel analyzed Fuchs's sign, preferring this term for the pseudo-Graefe phenomenon, and explained it as an accompaniment to an aberrant regeneration of the nerve fibers, occurring only with lesions which affect the trunk of the nerve. He stated that it was of the same nature as the Marcus Gunn phenomenon, in which fibers destined for the motor branch of the trigeminal nerve reach the oculomotor nerve. Gifford added that Voisin discussed Fuchs's sign and explained it as a synergy between the lower rectus muscle and the levator muscle of the eyelid, which is manifested when the eyes are opened after sleep. He expressed the belief that this synergic movement may in some cases persist when elevation of the eyelid is otherwise impossible. Coppez, cited in the same article, also preferred the denomination "Fuchs's sign" for the pseudo-Graefe phenomenon, he expressed the opinion that, the contraction being more accentuated when the patient looks downward and inward, aberrant regeneration of the fourth nerve may be considered a possibility. Gifford also cited Morax' case, in which, as in Halpern's case, there was no ptosis, the mobility of the eye was almost normal and retraction of the upper eyelid, when the patient was looking downward and inward, was the only anomaly present.

Sedan,⁶ in "*Traité d'ophtalmologie*," published under the auspices of the French Ophthalmological Society, presented A. Thomas' opinion on the subject, as follows:

When the ptosis is due to a total paralysis of the third pair of cranial nerves, there are sometimes noted, in the period of recovery, abnormal oculopalpebral synkineses, owing to errors in ligation (*erreurs d'aiguillage*) of the nerve fibers.

He stated, further, that Coppez defined Fuchs's sign as the ocular synkinesis consisting in elevation of the upper eyelid when the eye was looking downward and inward.

5 Gifford, S. R. Paradoxical Elevation of the Lid, *Arch. Ophth.* **22** 252-256 (Aug.) 1939.

6 Sedan, J., in Bailliant, P., and others. *Traité d'ophtalmologie*, Paris, Masson & Cie, 1939, vol. 3, p. 1065.

Yanes,⁷ of Habana, Cuba, published a case of incomplete paralysis of the left oculomotor nerve, in which the extrinsic musculature of the left eye was affected and the pupillary reflexes were preserved. Yanes was particularly aware that the ptosis was not a total one but disappeared completely when the right eye was occluded⁸ or when its vision was interfered with by a blinker or, again, when this eye was directed outward or inward. He compared his case and the case reported by Gifford and concluded that the possibility of the phenomenon being an accompaniment of aberrant regeneration of the nerve fibers, such as was present in Gifford's case, was doubtful in his case, in which simple occlusion of the right eye, without producing any movement of that eye, caused a retraction of the left upper eyelid. Though he stated at the beginning that he did not intend to place any pathogenic interpretation on the curious phenomenon but, rather, wished to assign one principle to the study of the complex topic of functional paralysis of the ocular muscles, he suggested, at length, the hypothesis of a sensory-motor association, adding, however, that any pathogenic interpretation placed thereon would be dubious and fallacious while there was no fundamental anatomic basis for it.

Rea⁹ cited a case of the pseudo-Graefe phenomenon. A patient aged 30, after a fracture of the base of the skull, had paralysis of the right oculomotor nerve and, as a residual of this, retraction of the upper right eyelid when looking downward and to the left. There was also contraction of the pupil of the right eye when the lid of this eye retracted.

Spaeth¹⁰ stated that Walsh and King, of Baltimore, were the first to call attention to the importance of the pseudo-Graefe phenomenon as a sign of intracranial saccular aneurysm. These authors¹¹ adopted the theory of defective nerve regeneration to explain the phenomenon and alluded to the publications of Bielschowsky, Bender Ford and Woodhall. Walsh and King, in a short series of cases of intracranial saccular aneurysm, discovered in 2 of them the concomitant occurrence

7 Yanes, T. R. Paradoxical Monocular Ptosis, *Arch. Ophth.* **23**:1169-1172 (June) 1940.

8 The same thing occurred in my case, as confirmed by *E* of the figure, but my patient, contrary to what Yanes stated with reference to his, perhaps through a natural effort to see with the left eye, moves her right eye after it has closed to force a retraction of the left upper lid.

9 Rea, R. L. *Neuro-Ophthalmology*, St. Louis, C. V. Mosby Company, 1941, p. 531.

10 Spaeth, E. B. *Principles and Practice of Ophthalmic Surgery*, ed. 3, Philadelphia, Lea & Febiger, 1944, p. 217.

11 Walsh, F. B., and King, A. B. Ocular Signs of Intracranial Saccular Aneurysms, *Arch. Ophth.* **27**:1-33 (Jan.) 1942.

of the pseudo-Graefe phenomenon. In 1 of these 2 cases besides retraction of the lid they noted a manifestation of defective nerve regeneration consisting in contraction of the paralyzed or parietic pupil on the effort of adduction. This manifestation they found also in 2 other cases of aneurysm, and I have already referred to it in discussing Bielschowsky's 5 cases, in 3 of which it appeared.

Adrogué¹² likewise discussed *fenómenos palpebrales*, which present themselves at times with incomplete recovery of paralysis of the oculomotor nerve, corresponding to the spasms of the levator of the eyelid, which always accompany such defective regeneration. He cited Bielschowsky's cases and Bielschowsky's explanation of the phenomenon and added:

This hypothesis of the pathogeny of the sign of pseudo "paradoxical monocular ptosis,"⁷ a term I prefer for the data presented by Gifford and Yanes, has been confirmed through the experiments on monkeys, carried out by Bender and Fulton,¹³ in which, in the anterior section of the oculomotor nerve, the nerve fibers regenerated along abnormal routes, producing the analogous phenomenon of retraction of the eyelid.

Prof. Linneu Silva, of Rio de Janeiro, examined my patient after I had determined the abnormal movement of the upper eyelid, and I wish to quote from his comment on the case:

The atypical recovery of function of the levator of the eyelid associated with impulses concerned with ocular position in which muscles innervated by the same pair of cranial nerves must participate, after iontotherapy and after a long period of complete inactivity of all the muscles innervated by the same nerve, suggests the persistence of fibers which are still capable of functioning and which, through synkinesis, conditioned to an increased inflow of nervous activity from impulses for the functioning of other muscles activated by the same nerve, enter into action. This mechanism is the more credible as the phenomenon is apparent in all directions of gaze in which the aforesaid muscles should participate, especially when a majority of them do so, as in adduction (which causes the strongest retraction of the lid), in which three components of the nerve receive the impulses.

TREATMENT

With regard to treatment, Spaeth¹⁴ advised:

In these instances the surgery first necessary is the correction of the residual lateral deviation, second, to dissect the entire levator free from the tarsal plate and the superior cul-de-sac, forming thereby a complete paralytic form of ptosis, third, the correction of this paralytic ptosis by the use of orbicularis fibers into

12 Adrogué, E. *Neurologia ocular*, Buenos Aires, El Ateneo, 1942, p. 127.

13 Bender, M. B., and Fulton, J. F. Factors in Functional Recovery Following Section of the Oculomotor Nerve in Monkeys, *J. Neurol. & Psychiat.* 2: 285-292 (Oct.) 1939.

14 Spaeth,¹⁰ pp. 219-221.

the occipito-frontalis, that is the Reese technique, and fourth, surgery to the superior and inferior recti on the opposite eye to limit their arc of contact—hence to limit their vertical excursion so that these will correspond more nearly with those pathologically limited excursions in the opposite paralyzed eye

SUMMARY

A case of grave disturbance of ocular motility is presented which supposedly conforms to those described under the denomination of "Fuchs's sign," "pseudo-Graefe phenomenon" or "pseudo-Graefe syndrome"

Only too evident are the absence of publication of similar cases in the many Brazilian journals of ophthalmology which I reviewed and the limited number of observations in foreign publications which I consulted. I enumerate, in condensed form and without comment, the cases I found in the literature and the theories on the pathogenesis of the phenomenon, and, finally, I indicate the treatment advised by Spaeth

BUPHTHALMOS IN A SIX MONTH PREMATURE INFANT

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AND
ABRAHAM KORNZWEIG, M D
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INFANTILE glaucoma, or buphthalmos, has been discovered occasionally in newborn infants at term¹ The present case is of special interest because it affords an opportunity to study congenital glaucoma in microscopic section at an earlier stage than has hitherto been possible On section, it was found to belong to the small group of cases of buphthalmos characterized by absence of Schlemm's canal, complete anterior iris synechias and very shallow or no anterior chamber These anatomic features were striking in comparison with the deep anterior chamber and hydrophthalmos more commonly found in cases of congenital glaucoma

REPORT OF A CASE

History—The circumstances in which the globes of the 6 month premature infant were obtained were interesting During the spontaneous birth of the infant the cornea of the right eye ruptured On examination two hours later, the left eye was observed to be stony hard and the cornea milky white, but the cornea did not appear to be enlarged The child died several hours later Both eyes were removed soon after death They were fixed in Bouin's solution, and serial sections were prepared in paraffin and stained with hematoxylin and eosin and with Weigert's method for elastic tissue

Figure 1 indicates the occurrence of familial congenital glaucoma in 3 other members of the family of the mother of the premature infant In the table, measurements of the enlarged left eye are compared with those of the eye of a normal 6 month old fetus

Microscopic Study of the Eye—Right Eye (fig 2) Except for the rupture of the cornea and the extrusion of retina, the right eye was normal in all respects Schlemm's canal was well developed, trabeculated tissue in the angle was properly differentiated, and the iris was fully grown There were no defects or thinning apparent in the sclera There were no abnormalities of the retina or the choroid or evidences of intraocular hemorrhage The cause of the rupture of the globe was not determined

From the Laboratories and Ophthalmological Division of the Mount Sinai Hospital

^{*} Read before the New York Academy of Medicine, Section of Ophthalmology, Jan 21, 1946 A discussion of this paper, under the title "Glaucoma in a Premature Infant Report of a Case" appeared in the August 1946 issue of the ARCHIVES, page 241

1 Anderson, J R Hydrophthalmia, or Congenital Glaucoma Its Causes, Treatment and Outlook, London, Cambridge University Press, 1939

Left Eye The left eye, uniformly enlarged in all its diameters, appeared round, rather than elongated and oval. This was in striking contrast to the usual appearance of buphthalmic eyes, in which the enlargement of the anterior segment is most prominent. As compared with a normal fetal eye of the same age, the distention of the cornea was indicated by the obliteration of the anterior corneoscleral sulcus, producing a uniformly rounded appearance.

Cornea The corneoscleral junction was barely indicated. There was practically no difference in the radius of curvature of the cornea and that of the sclera.

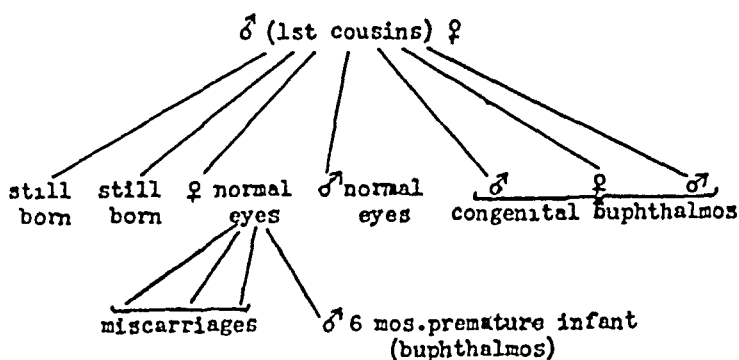


Fig 1—Ocular history of the family of a 6 month premature infant, indicating familial congenital glaucoma

The epithelium was three layers in thickness. Bowman's membrane was perceptibly thinned. Many of the stroma cells were swollen. Descemet's membrane was present, but the endothelium of the central portion of the membrane had been displaced. It was observed on the anterior capsule of the lens, indicating that the lens had been in contact with Descemet's membrane.

Measurements, in Millimeters, for the Enlarged Eye of a Six Month Premature Infant with Buphthalmos Compared with Those for the Eye of a Normal Fetus of the Same Age

	Normal 6 Mo—Fetus	6 Mo—Prema- ture Fetus with Buphthalmos
Anteroposterior diameter of globe	10.5	15
Transverse diameter of globe	10.0	14
Transverse diameter of cornea	6.0	9
Thickness of cornea at center	0.8	0.3
Thickness of cornea at limbus	0.86	0.4
Thickness of sclera at limbus	0.36	0.28
Thickness of sclera at equator	0.3	0.1
Thickness of sclera at posterior pole	0.6	0.36

Iris The iris was adherent to the posterior surface of the cornea in its entire extent. It was much thinner than normal, but its development corresponded to that of the iris of a 6 month old fetus. This was indicated chiefly by the fact that the pigment of the posterior layers of the pigment epithelium had progressed to the base of the iris at the ciliary body. Some fibers of the pupillary membrane could be seen at the tip of the iris. Interposed between the endothelium of the iris and Descemet's membrane was a hyaline membrane. This membrane was bordered on either side by a thin, flat layer of endothelial cells. It stained faintly.

lavender with hematoxylin and eosin and extended from the base of the iris almost to the pupillary margin, gradually thinning as it approached the center of the cornea. There was a faint suggestion of Schlemm's canal on one side of

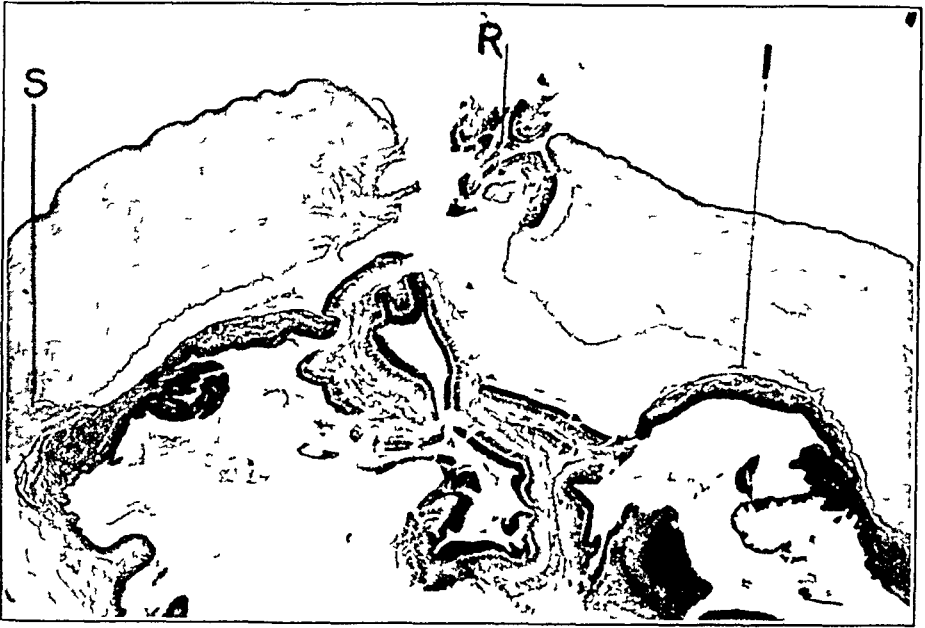


Fig 2—Right eye of the buphthalmic fetus, which was normal except for spontaneous corneal rupture at birth. *S* indicates Schlemm's canal, *I*, normal iris, *R*, site of corneal rupture.

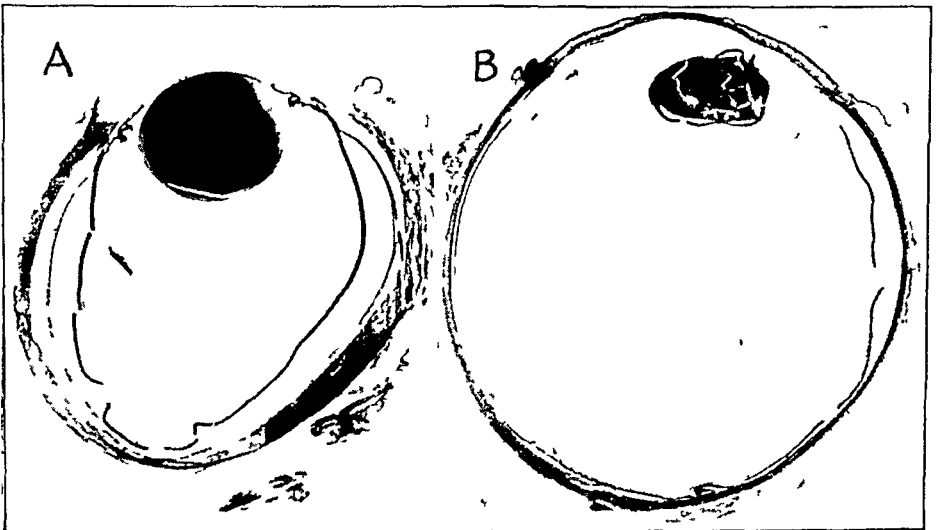


Fig 3—Early buphthalmos of the left eye, *B*, compared with the smaller eye, *A*, of a normal 6 month old fetus.

the cornea, but not on the other. The site of the angle was blocked on both sides, the ciliary body lying on one side and the root of the iris on the other.

Ciliary body. The ciliary processes were considerably flatter and fewer than normal. The pars planum was considerably longer than normal for an infant.

of this age The ciliary muscle was also flattened Meridional and radial fibers could be seen, but circular fibers were absent

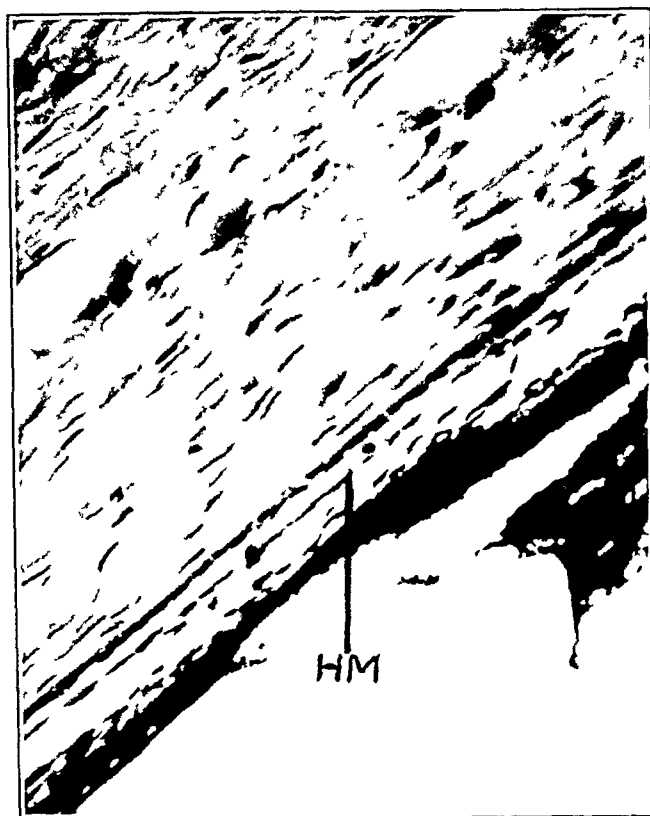


Fig 4—Hyaline membrane, *HM*, interposed between Descemet's membrane and the anterior layers of the iris

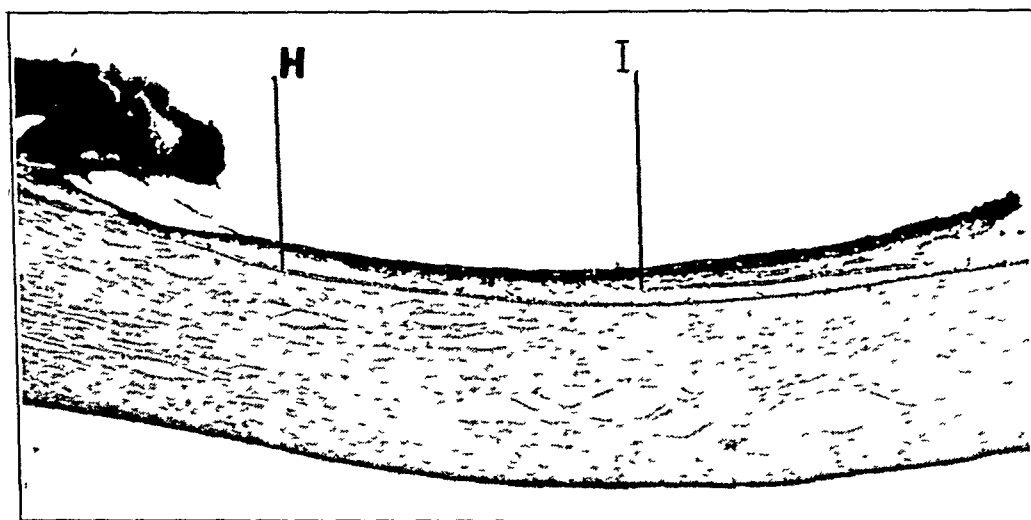


Fig 5—Site of angle, indicating absence of trabeculated structure and adhesion of the iris to the corneoscleral junction *I* is the iris, *H*, the hyaline membrane

Lens The lens was displaced forward It was smaller and flatter than normal for an infant of this age but showed normal arrangement of fibrils There was no evidence of the hyaloid artery or its branches posteriorly

Retina The retinal elements were in their third stage of development. All the layers were present but not fully matured. The macula was not examined. There was no evidence of retinal atrophy or compression of the layers. The optic disk showed early glaucomatous cupping. There was no evidence of the hyaloid artery or of its sheath.

Choroid This layer was thinner than normal. There were fewer blood vessels than are normally seen. The lamina suprachoroidea either was absent or had been completely obliterated.

Sclera The sclera was uniformly reduced in thickness (fig 3). It was thicker posteriorly than at the equator or at the corneoscleral junction.

COMMENT

Of clinical interest in the case of this premature infant with buphthalmos is the presence of a hereditary tendency, to familial congenital

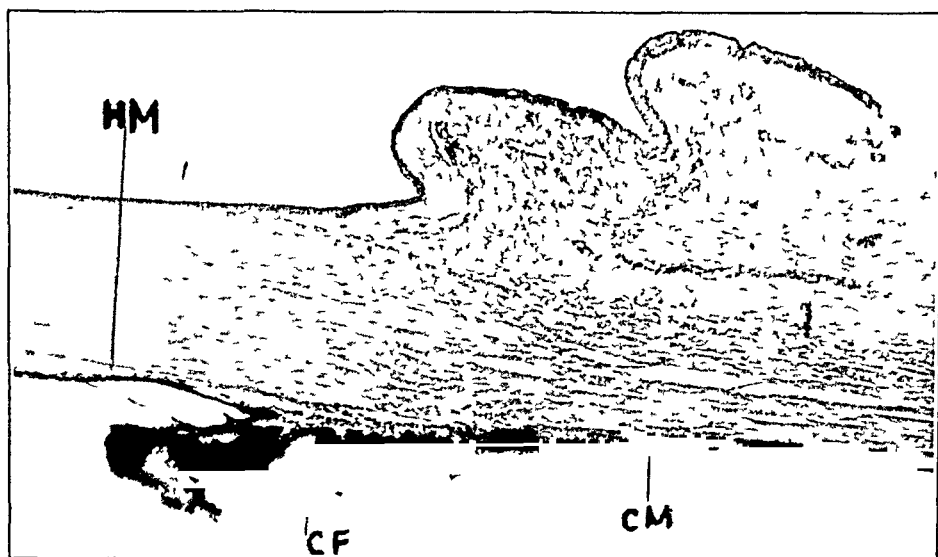


Fig 6—The ciliary processes, *CF*, are flattened, the ciliary muscle, *CM*, is thin and elongated. *HM* is the hyaline membrane.

glaucoma and of consanguinity of the grandparents. Duke-Elder² stated that consanguinity is a factor in 10 per cent of cases of congenital glaucoma.

Most observers point to a persistence of the prenatal condition of the mesoderm in the region of the corneoscleral junction as being responsible for the obstruction to drainage of intraocular fluid, and hence for the eventual development of buphthalmos. If this is true, it did not affect the normal growth and development of the iris in the present case. What remains to be explained is whether the adhesion of iris to cornea is a primary condition (i.e., persistence of the early fetal condition) or

² Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1938, vol. 3, pp. 1295 and 1297.

whether it is a result of intraocular tension. The presence of a hyaline membrane on the surface of the iris, while of particular interest, does not help in the solution of this problem. A hyaline membrane, as Mann³ suggested, tends to form when cornea and iris stroma remain too long in contact. However, one cannot exclude the development of such a membrane as a reaction of the fetal iris to increased intraocular pressure. The role of inflammation as a cause of iris synechia and of the hyaline membrane is, of course, to be considered. It cannot be excluded as a factor in this case merely because the sections did not reveal evidences of inflammatory disease. Herbert⁴ has emphasized the importance of inflammation in the formation of such membranes in the adult eye.

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3 Mann, I C. *Developmental Abnormalities of the Eye*, London, Cambridge University Press, 1937, p. 295.

4 Herbert, H. Glass Membrane Formation in Chronic Iridocyclitis, *Tr. Ophth Soc U Kingdom* 47:155, 1927.

PATHOGENESIS OF GLAUCOMA AND "GLAUCOMATOUS" ATROPHY OF THE OPTIC NERVE

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SOME investigators, Fuchs¹ for example, have called attention to certain congenital anomalies of the glaucomatous eyeball. A characteristic small bulbus, a shallow anterior chamber, bulging ciliary processes and a comparatively large lens are met with in glaucoma. The higher incidence of "inflammatory" glaucoma in hyperopic persons may point in the same direction. In hydrophthalmos the ligamentum pectinatum and the angle of the anterior chamber are originally underdeveloped. The lens is rather small. Bilateral spherophakia, with a congenitally weak zonula, may be complicated by glaucoma, as Bowman noted. All these anomalies mean a developmental peculiarity or disproportionate growth of the various tissues of the bulbus. According to studies which I have carried out in recent years, to be published elsewhere, proportionate physical growth is related to the normal activity and normal development of the central nervous system, including the pituitary body and the epiphysis. The eyeball, the optic nerve and the ciliary ganglion—the main factors involved in the pathogenesis of glaucoma—belong embryologically to the brain. Some relation between the development of these structures and that of the brain may therefore be anticipated. The anatomic peculiarities of the glaucomatous bulbus might lead one to suspect an anomaly of the central nervous system. This view has to some extent been corroborated by the studies on heterochromia of the iris (Hess³). This congenital anomaly of the iris is associated with a special type of skull (eurycephaly) and with lesions of the spinal cord, the latter belonging to the status dysraphicus (Bremer⁴). In some cases of hydrophthalmos, furthermore, the congenital glaucoma, port wine stains (hemangioma congenitale) of the skin of the face and an anomaly of the brain—angiomas in the meninges and in the cortex—are frequently encountered. In other instances of

1 Fuchs, E. *Lehrbuch der Augenheilkunde*, ed 16, Vienna, Franz Deuticke, 1940, p 445

2 Bowman, W. Roy. *London Ophth Hosp Rep* **1** 1, 1865, cited by Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1941, vol 3, p 331

3 Hess, L. *Heterochromia of Iris*, *Arch Ophth* **30** 93 (July) 1943

4 Bremer, F. W. *Deutsche Ztschr f Nervenhe* **95** 1, 1926, **99** 104, 1927

hydiophthalmos, multiple neurofibromas, prominent asymmetry of the face (hemihypertrophy) and megalophthalmos have been reported. It is tempting to recall in this connection Bourneville's tuberous sclerosis, with its neuroglial growths both in the hemispheres and in the retina, and Lindau's disease, the interesting coincidence of retinal tumors and tumors of the same structure within the central nervous system (cerebellum, pons and temporal lobes), the brain and retina being the exclusive site of these angiomatous lesions. It may be mentioned in passing that formation of cysts and of cavities is a significant feature of Lindau's disease. To Schnabel⁵ credit is due for having noted cavities in the anterior part of the optic nerve, which he stated to be a characteristic of glaucoma. This statement has been questioned. In any case, the congenital anomalies of the bulbus (Bowman² and Fuchs¹), and possibly Schnabel's cavities, are suggestive of an organic, anatomic or constitutional peculiarity. Two problems arise at this point. 1. Is it merely a local anomaly of the eye, or is it a cerebral, neural anomaly, which underlies glaucoma, and eventually the glaucomatous atrophy of the optic nerve? If the latter, the recognition of the neural or constitutional peculiarity would provide a clue both to the pathogenesis and to the diagnosis and prognosis of glaucoma. The liability of the Jewish people to glaucoma, for example, may have a certain nervous or constitutional basis. A familial incidence of glaucoma has been reported by some authors. In 50 per cent of descendants of patients with glaucoma, Schoenberg⁶ noted a surprising response to instillation of epinephrine into the conjunctiva (epinephrine mydriasis). This unusual response is a sign of a lesion of the third neuron in the sympathetic pathway of the pupil (Hess⁷). This lesion either is acquired after surgical intervention or is a sign of an inherited neural anomaly. 2. If there exists any relationship between the eye and the brain aside from the well known mechanical one (increased intracranial pressure and papilledema), is it not possible that by studying certain nervous disorders which are known often to be complicated by atrophy of the optic nerve, as glaucoma sometimes is, one might obtain a better insight into the mechanism of glaucoma as well as of glaucomatous atrophy of the optic nerve? Disregarding, in this article, the cupping of the disk, which represents in itself a difficult problem, and considering only the so-called primary atrophy of the optic nerve, one must emphasize again that the significant signs of glaucoma cannot be satisfactorily accounted for without digging more deeply and without attempting to define better what happens below the surface, i. e., behind the eyeball, the apparent scene of the clinical events.

5 Schnabel, J. *Ztschr. f. Augenh.* **14** 1, 1905, **19** 556, 1908

6 Schoenberg, M. *Tr. Am. Ophth. Soc.* **22** 53, 1924

7 Hess, L. *Epinephrine Mydriasis*, *Arch. Ophth.* **30** 194 (Aug.) 1943

At the very outset, one should keep in mind the following facts, which demonstrate that the close relation that is assumed to exist between the atrophy of the optic nerve and the increased intraocular pressure appears to be doubtful

1 Despite sustained high intraocular pressure, atrophy of the optic nerve may not occur for a long time

2 There is no definite or constant correlation between the amount of intraocular pressure and the atrophy of the optic nerve This would conform to clinical experience in other fields There is, for example, no correlation between the level of systolic blood pressure and the hypertrophy of the left ventricle, the latter being dependent on many factors besides the arterial hypertension (Hess⁸)

3 Despite lowering of the intraocular pressure by adequate and timely treatment, progressive atrophic changes may ensue

4 Atrophy of the optic nerve may develop in glaucoma even though intraocular pressure is never greatly increased

In view of the anatomic facts noted in glaucomatous eyes by Bowman, Fuchs and Schnabel, and in view of these clinical observations concerned with atrophy of the optic nerve, the following questions deserve attention

1 In what circumstances is one accustomed to see "primary" atrophy of the optic nerve?

2 If, in accordance with the discussion in the second article in this series,⁹ the primary site of glaucoma is assumed to be in the nervous system, behind the bulbus, are any morbid changes of retrobulbar origin known to be associated with primary atrophy of the optic nerve, except for traumatic injuries and all conditions exerting mechanical pressure on the optic nerve (intracranial, intraorbital and intraocular pressure)? If so, what, precisely, is the site? What is the pathologic picture?

In passing, it might be mentioned that the ventrotemporal part of the optic nerve rests on the internal carotid artery A sclerosed carotid artery, aneurysm of the arteria communicans anterior and sclerosis of the circle of Willis are recorded in the literature (Knapp¹⁰) to have caused bilateral atrophy of the optic nerve This mechanical factor will not be discussed at length in this article

Bilateral atrophy of the optic nerve associated with (a) growths arising from the pituitary body or its surroundings (suprasellar, infrasellar and presellar tumors), (b) arachnoiditis interchiasmatica cystica

8 Hess, L Ztschr f Constitutionslehre 9 1 and 72, 1923

9 Hess, L Pathogenesis of Acute Glaucoma, Arch Ophth 32 128 (Aug) 1944

10 Knapp, A Association of Sclerosis of Cerebral Basal Vessels with Optic Atrophy and Cupping Report of Ten Cases, Arch Ophth 8 637 (Nov) 1932

or (c) lesions of the pregeniculate tract is generally believed to be due to pressure exerted on the optic nerve fibers. Obliteration of the cisterna chiasmatica, above which the chiasm rests (Hirsch¹¹), failure of the frontal arachnoid spaces to fill with air, and displacement of the ventricles, as seen in encephalograms, are considered objective signs of abnormal increased pressure within the cranium. The mechanism of this pressure, which undoubtedly is present in the advanced stages, has been explained by Hirsch¹¹. Schnabel,¹² on the other hand, was impressed by the early and abrupt onset in certain cases of bitemporal hemianopsia which could not be accounted for by mechanical pressure and, furthermore, by the distinct, sharp demarcation of the nasal and the temporal half of the visual fields. It is to be borne in mind that in some instances of infrasellar tumor, according to personal experience, a central scotoma may represent an early sign of this disease, prior to the development of bitemporal hemianopsia and signs of increased pressure. The well known fact that papilledema is rather uncommon with tumors of the pituitary body (except for presellar growths) could not be satisfactorily explained. It might, therefore, be advisable to recall Schnabel's¹² suggestion that not the mechanical factor—or not such a factor exclusively—but some toxic, endocrine or congenital agent may play a role in the pathogenesis of hemianopsia and atrophy of the optic nerve.

From Hirsch's¹¹ important work on the hypophysis an amazing fact emerges. In cases of tumor of the hypophysis without definite signs of acromegaly, Hirsch noted visual disturbances in 100 per cent and primary atrophy of the optic nerve in 89 per cent. In contrast to this, in cases of tumors associated with undoubted acromegaly, ocular signs were noticeable in about 50 per cent. Tumors of the latter category are mainly confined to the sphenoid bone and rather rarely grow toward the brain. So long as the tumor does not reach the floor of the brain, and remains confined to the sphenoid bone, there are no ocular disturbances. On the other hand, there are certain instances (of the "ocular type," according to Hirsch¹¹), in which impairment of sight is an early sign. The coincidence of these ocular signs with sexual disturbances (impotency, menopause, loss of hair, milk in the mammary glands), and sometimes with adiposity, is impressive. The conclusion to be drawn is this. According to Erdheim,¹³ the genital dystrophy as well as the adiposity are due to a destructive lesion within the hypophysiodiencephalic system (in the hypophysis or in the interbrain or in both) and is not a sequel of the eosinophilic hyperfunction of the anterior lobe. Consequently, the association of the genital signs with

11 Hirsch, O. *Wien klin Wchnschr* **36** 93, 1926, *Ztschr f Augenh* **45** 294, 1921, *Presse méd* **34** 578, 1926.

12 Schnabel, V. *Sitzungsb d Wien ophth Gesellsch*, Nov 16, 1904.

13 Erdheim, J. *Beitr z path Anat u z allg Path* **46** 233, 1909.

atrophy of the optic nerve suggests that the latter may to some extent be related to the cerebral factor, and not exclusively to the mechanical pressure. The persistent ductus craniopharyngeus in some cases of tumor of the hypophysis is evidence of a congenital anomaly of the sphenoid bone or of the middle fossa, as in hypertelorism, which will be discussed soon. From a diagnostic standpoint, it may be mentioned that, according to Hirsch, early temporal hemianopsia for colors was found in only a single case of tumor of the hypophysis with acromegaly.

It is a matter of clinical experience that in cases of disturbances of the pituitary body, hypermetropia, myopia of a high degree, astigmatism and strabismus are of frequent occurrence, indicating a congenital anomaly of the eyeballs. The same holds true of arachnodactyly.

In arachnodactyly (Marfan¹⁴) an anomaly of the skeleton ("spider fingers") and disproportion between the length of the extremities and the height is coupled with pronounced ocular defects (bilateral dislocation of the lens, iridodonesis, lenticular and axial myopia, as high as from 40 to 60 D, miosis, and slanting of the palpebral fissure). The sella turcica may be reduced in size and the clinoid processes thickened and bridged. In Schilling's¹⁵ case, a fast growing boy, with a height of 172 cm at the age of 14, had extremely dry skin, with pronounced striae distensae (such as is associated with Cushing's basophilic adenoma of the anterior lobe of the pituitary), and scanty formation of hair on the chest and in the axillae. Later the picture of Friedreich's disease developed. A certain degree of hypertelorism and a massive chin were reported in several instances. In 1 of my cases, that of a woman aged 20, the menarche occurred late (at the age of 17) and the flow was scanty. The lower portions of the legs and the sacrum were hairy. All these signs are indicative of involvement of the middle fossa (including the hypophysis and the diencephalon). The lack of pupillary response to atropine and the miosis (Rados¹⁶) are also suggestive of a disturbance of the vegetative nervous system, which may be traced back to the central, diencephalic lesion.

Important in this discussion, for many reasons, is the problem of retinitis pigmentosa. They may be enumerated as follows:

1 The constant, clinical coexistence of ocular changes, obesity and hypogenitalism (de Schweinitz¹⁷). This holds true for all types, not for the well known Laurence-Biedl syndrome only. This fact, together with the occasional initiation or acceleration of the symptoms with

14 Marfan, A. B. Bull et mem Soc med d hôp de Paris **13** 220, 1896

15 Schilling, V. Med Welt **1** 219 (Feb 15), 259 (Feb 22) 1936

16 Rados, A. Marfan's Syndrome (Arachnodactyly Coupled with Dislocation of Lens), Arch Ophth **27** 477 (March) 1942

17 de Schweinitz, G. E. Tr Am Ophth Soc **10** 228, 1904

pregnancy (Henderson¹⁸) indicates a relationship to the pituitary-diencephalic area. I shall come back to this point in discussing amblyopia graviditatis. In the literature, onset of signs following the acute exanthems has been reported. This observation could be interpreted as a result of a concomitant encephalitic lesion, which is known to be commonly associated with many infectious conditions. The almost invariable bilaterality of the disorder is additional evidence of a central origin. The dorsum sellae appears to be thick and unusually steep.

2 The association with myopia of a high degree

3 The occasional association with Friedreich's disease. In this disease involvement of the interbrain cannot be doubted.

4 The clinical coincidence with diencephalic signs and with bilateral atrophy of the optic nerve.

5 The coexistence with painful intestinal spasms, which can be controlled only with the use of epinephrine, a phenomenon indicative of a disturbance of the sympathetic nervous system. It may be recalled that an important vegetative center is located in the diencephalon (Karpplus and Kreidl¹⁹ and Ranson²⁰).

6 The association with tabes dorsalis (Katzenstein).

7 The association with glaucoma.

British authors have noted that families tainted with retinitis pigmentosa are surprisingly prolific. According to Nettleship²¹ there is an average of nine children to each marriage. In the light of these considerations, the clinician is driven to three conclusions:

1 Retinitis pigmentosa is a congenital anomaly, as evidenced by heredity and the associated congenital disorders (obesity and genital hypoplasia in all cases, polydactyly in cases of the Laurence-Biedl type). The onset of symptoms, however, is often precipitated by a factor acting on the central nervous system (acute exanthems).

2 Retinitis pigmentosa may be traced back to a primary disturbance of the diencephalon, the retina and the optic nerve being derivatives of the diencephalon. It is noteworthy that the hypophysis appears to be developed at about the eighth week of embryonic life. At the same time—about the third month—the rods make their appearance. The rods are first involved by the disease process. At about the eighth week a center appears at the base of each great wing of the sphenoid bone,

18 Henderson, R. H. Retinitis Punctata Albescens, and Retinitis Pigmentosa as Affected by Pregnancy. Report of a Case, *Arch. Ophth.* **11**:763 (May) 1934.

19 Karpplus, J. P., and Kreidl, A. *Arch. f. d. ges. Physiol.* **129**:138, 1909, **135**:401, 1910, **143**:109, 1911, **171**:192, 1918.

20 Ranson, S. W., in *Harvey Lectures, 1936-1937*, Baltimore, Williams & Wilkins Company, 1937.

21 Nettleship, E. *Tr. Ophth. Soc. U. Kingdom* **7**:301, 1887, **29**:128, 1909.

as well as a pair of centers in the body of this bone (Morris²²) A disturbance at this period of embryonic life could account for all the signs of this disease

3 Atrophy of the optic nerve in retinitis pigmentosa, or the "anlage" to the atrophy, is of central origin Its progressive habit is in line with the progressive tendency of other congenital nervous anomalies, the optic nerve being actually not a peripheral nerve but, rather, a nerve tract

No nystagmus or sign of status dysraphicus or increased intraocular pressure has been noted in association with retinitis pigmentosa

As an illustration of these conclusions, a case studied at the Wrentham State School and that of an older patient may be mentioned

A youth aged 18, a moron, had bilateral retinitis pigmentosa (or syphilitic chorioretinitis ?)²³ There was no familial incidence of the disease The Wassermann-Hinton reaction of the blood was negative He presented obesity of female type and gynecomastia The pubic hair was scanty, with a horizontal hair line, the arm pits and all the extremities were hairless

A woman aged 54 presented a virile appearance (strong chin, large toes) The menarche occurred late, at the age of about 17, and there was a tendency to obesity Hypertrichosis was present The patient was practically blind, as was her sister, due to bilateral atrophy of the optic nerve She presented a classic picture of retinitis pigmentosa

In studying a group of about 80 children with mongolism in the Wrentham State School, I noted a tendency to obesity in a certain percentage, the distribution of the fat reminding one of the Frohlich type, with retarded sexual development, hyperopia or myopia of a high degree and sometimes strabismus The irises were often blue According to Benda,²⁴ there is ample evidence of a histologic anomaly of the pituitary body in mongolism In line with this is the hypoplasia of the subthalamie region and of the corpora mamillaria observed in persons with mongolism by van der Scheer²⁵ In 1 case Greig²⁶ noted premature synostosis spheno-occipitalis, and in another, a shallow sella, only 5 mm in depth, the dorsum sellae being small and the posterior clinoid process not developed These findings, in my opinion, indicate an anomaly of the middle fossa Greig,²⁷ however, expressed the belief "that the defects through the skull were coincident and proportionate, and that no area

22 Morris, H Human Anatomy, edited by J P Schaeffer, Philadelphia, The Blakiston Company, 1943, p 1390

23 Dr N S Riemer furnished the data on the eyes

24 Benda, C E Studies in Mongolism III The Pituitary Body, Arch Neurol & Psychiat 42 1 (July) 1939

25 van der Scheer, cited by Kreyenberg, G, in Bumke, O, and Foerster, O Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol 16, p 24

26 Greig, D Edinburgh M J 34 253, 1927

27 Greig, D Edinburgh M J 31 560, 1924

seemed to present a primary disturbance" Atrophy of the optic nerve has not been reported in persons with mongolism My clinical observations revealed signs of status dysraphicus This is an important fact to be considered in drawing further conclusions In any case, in mongolism a histologically abnormal pituitary body is associated with an underdeveloped diencephalon, with sexual retardation and with anomalies of the eye

Underdevelopment of the middle cranial fossa, together with excessive smallness of the greater wings of the sphenoid bone, persistence of the primitive craniopharyngeal duct and external bilateral squint and atrophy of the optic nerve are encountered in hypertelorism (Greig²⁷) Sexual development in this disease is again retarded, the "full moon" face is similar to that in Cushing's cases of basophilic tumors of the hypophysis The initial lesion, in contrast to that associated with mongolism, is limited to a small area of the cranium, involving chiefly the middle fossa In comparison with the large recesses for the cerebellar lobes, the lateral recesses in the middle fossa appear small, although not shallow, as in hydrocephalus The sella turcica is large and forms a cuplike depression Each optic foramen is large and triangular There are no signs of intracranial pressure The impression is that of a localized ("segmentary"?) lesion There are no signs of status dysraphicus, which apparently is not at the basis of this disease

Primary atrophy of the optic nerve is not unusual in cases of Friedreich's disease (Guillain²⁸) No explanation of this association has been given in the literature, the interest of most authors being centered on the congenital lesions of the spinal cord and of the cerebellum In a famed case described by Friedreich²⁹ himself, he noted diabetes insipidus, salivation, "unmotivated" diarrhea, sweating and palpitation—exactly the signs mentioned by Karplus and Kreidl¹⁹ in their experiments on the diencephalon The menarche is often late, and sexual impotency is often reported Impressive in some cases (in 2 of my observations) is the athletic musculature The occurrence of laryngeal crises, of polyuria and glycosuria, of choreic, athetoid and ticlike movements (noted by me) and of *Torsionsspasmus* and nanosomia, and, furthermore, the adiposity and puffiness of the face, the hypoplasia and infantilism, as well as anatomic investigations, all furnish evidence that the histologic changes extend up to the fourth ventricle, to the nucleus ruber and the tegmentum, i e., to the diencephalon In 1 case (Friedreich²⁹) a cyst was observed in the hypophysis Ferguson and Critch-

²⁸ Guillain, G Études neurologiques, Paris, Masson & Cie, 1936, series 7, p 134

²⁹ Friedreich, N Virchows Arch f path Anat **26** 391, 1863, **68**:145, 1876, **70**:140, 1877

ley³⁰ compared the atrophy of the optic nerve with Leber's hereditary optic nerve atrophy. It might be wiser to trace the atrophy under discussion to a diencephalic lesion. In 4 cases of Friedreich's disease studied in the Wrentham State School, the skull, particularly the forehead, was very high, reminding one of oxycephaly.

Of definite interest in arriving at a conclusion are observations on patients with oxycephaly ("tower skull"), a condition which is often associated with bilateral atrophy of the optic nerve. There is a divergence of opinion as to the origin of the atrophy, but Marchesani³¹ expressed the belief that it is "primary" and not neuritic. The origin of this atrophy has been accounted for by pressure on the optic nerves. The optic foramina, however, are not narrowed, as observed at autopsy. As for the role of internal hydrocephalus, evidenced by markings on the inner table of the cranium and the occasional hypertension of the cerebrospinal fluid, it should be kept in mind "that much severer cases of that pathological state occur in infancy and childhood without optic atrophy" (Wilson³²). The predominant anatomic feature of oxycephaly is a considerable depression of the middle fossa, with the sella descending to the level of the cerebellar fossa (Bertolotti's basilar lordosis). It is more likely that this initial dysgenesis of the sphenoid bone and of the sella is connected with changes in the pituitary gland and in the eyes. Outstanding in the clinical picture are three features: (1) bilateral atrophy of the optic nerve, (2) the frequent occurrence of divergent squint (as in hypertelorism) and (3) the occurrence of dyspituitarism, which in general has been disregarded in the writings of authors. In 1 of my cases, that of a man aged 68, deposits of fat were present on the thighs, the lower abdominal wall and the inner aspect of both arms. The pelvis was large and of the female type. There was gynecomastia, and the limbs and chest were hairless. The pubic hair line was horizontal. In cases recorded by Kretschmer,³³ eunuchoidism, homosexuality and hypoplasia of the testes and of the genitalia were manifest. In 2 of my cases the chin was slightly receding and was high and strong, similar to the chin of acromegaly, the incisors of the upper jaw were separated, the hair of the eyebrows was thick and rough, and the hair of the scalp was dense, thick and brittle. The underdevelopment of the sexual glands, the preponderance of males (all my 4 patients were males) and the peculiarity of the chin and hair are suggestive of a disorder of the

30 Ferguson, T. R., and Critchley, M. J. *J. Neurol. & Psychopath.* 9:120, 1928.

31 Marchesani, O., in Bumke, O., and Foerster, O. *Handbuch der Neurologie*, Berlin, Julius Springer, 1936, vol. 4, p. 107.

32 Wilson, S. A. K. *Neurology*, edited by A. N. Bruce, Baltimore, William Wood & Company, 1940, vol. 2, p. 1444.

33 Kretschmer, E. *Körperbau und Charakter*, Berlin, Julius Springer, 1936, p. 75.

pituitary gland Dollinger³⁴ reported a case of oxycephaly with Frohlich's adiposogenital dystrophy In all likelihood, the physician is confronted in cases of oxycephaly with a syndrome composed of changes in the skull, dyspituitarism and atrophy of both optic nerves The anatomic changes begin at the base of the skull There are no signs of status dysraphicus, so far as my personal experience goes Clinically, there is no nystagmus (Brunner³⁵), unless exceptionally, as a result of amblyopia

During pregnancy an enlargement of the hypophysis always takes place, and it is probable that the sudden onset of amblyopia or blindness (amblyopia graviditatis) observed in some instances, and relieved immediately after delivery (Weigelin³⁶), is related to the hypophysis Furthermore, bilateral hemianopsia has been observed During lactation, amblyopia may occur Mechanical pressure in these circumstances cannot be questioned On the other hand, profound endocrine changes, originating probably in the pituitary body, are taking place The sudden onset of visual disturbances reminds one of Schnabel's¹² comment Many signs similar to acromegaly, such as coarsening of the features, a tendency to glycosuria and exaggerated libido, are present In rare instances, recorded in the literature, attacks of glaucoma have first been observed during pregnancy and have ceased after delivery or soon after abortion, i e., at a time when the size of the hypophysis could hardly have been reduced

In certain instances of infantile myxedema, bilateral primary atrophy of the optic nerve has been reported No explanation of this has been found in the literature It is noteworthy that even when the hypophysis is not enlarged a large number of Erdheim's pregnancy cells can be demonstrated in the anterior lobe This rather constant observation may call to mind the transient ocular disturbances during pregnancy previously mentioned A profound endocrine imbalance is common to the two conditions It might, to a certain extent, corroborate Schnabel's¹² suggestion of an endocrine origin of visual defects in some cases of pituitary disorders In infantile myxedema there are no signs of increased intracranial pressure In this condition organic involvement of the pituitary body is again associated with genital underdevelopment—a constant anatomic disorder in myxedema infantum—and with bilateral atrophy of the optic nerve Many authors (Pineles³⁷) believe

34 Dollinger, cited by Schob, F G, in Kraus, F, and Brugsch, T *Spezielle Pathologie und Therapie*, Berlin, Urban & Schwarzenberg, 1921, vol 10, chap 3, p 873

35 Brunner, H, in Alexander, G, and Marburg, A *Handbuch der Neurologie des Ohres*, Berlin, Urban & Schwarzenberg, 1924, chap 1, p 985

36 Weigelin, S *Arch f Augenh* 61•1, 1908

37 Pineles, F *Wien klin Wchnschr* 1902, no 43

the disease to be a congenital disorder (thyreoplasia congenita) It is probable that the atrophy of the optic nerve represents a congenital anomaly As the parathyroid is intact, there is no cataract, in contrast to tetany, with its involvement of the parathyroid and the frequent occurrence of lenticular disturbances.

COMMENT

It might be advisable to call to mind the well known signs of primary atrophy of the optic nerve pallor of the disk, developing simultaneously, or within a short interval, in the two eyes; its progressive character, and the early impairment of eyesight There is no evidence of any preceding inflammation (of the eyeball, the orbit, the optic nerve or the brain and its membranes) or of mechanical pressure All these classic signs are consistent with the picture of a "central" congenital disturbance In the conditions discussed the ocular signs coincide with (*a*) gross anatomic changes of the middle fossa, including the pituitary body and its surroundings (pituitary tumors, arachnoiditis interchiasmatica, oxycephaly, hypertelorism and Friedreich's disease), and (*b*) functional disturbances of the pituitary body and the diencephalon (arachnodactyly, retinitis pigmentosa, myxedema infantum, pregnancy and lactation)

Structural Changes—As has been mentioned, it is noteworthy that no signs of hydrocephalus or increased pressure are evident The changes are located at the junction of the notochordal and the trabecular region of the cranium, since in the embryo the notochord extends only as far as the hypophysial fossa The development of this section of the cranium, especially of the sphenoid bone, is highly complicated Membranes and cartilages participate in its formation Five centers are required to form the anterior, or presphenoidal, portion from the original cartilage, whereas the postsphenoidal portion is partly of membranous and partly of cartilaginous origin Developmental disorders of this part of the skull, together with disorders of the nerve tissues adjoining, may easily take place, the skull and the central nervous system actually representing one unit (Erdheim³⁸) It is not without interest that, according to Hochstetter,³⁹ in early embryonic life the roof of the hypophysis and the floor of the interbrain are in intimate contact and that in later stages a connective tissue between the two can be detected As this disturbance of growth concerns only the prechordal part of the cranium, only the nose and eyes, the telencephalon and the thalamencephalon are involved This primary disorder concerns a minute, circumscribed portion of the floor of the cranium, the sequelae are far reaching On the other hand,

38 Erdheim, J Virchows Arch f path Anat **301** 763, 1938

39 Hochstetter, F Beiträge zur Entwicklungsgeschichte des menschlichen Gehirns, Vienna, Franz Deuticke, 1924, vol 2, p 2

under the category of "hypostosis," according to Hess,⁴⁰ are to be summarized a host of congenital anomalies, such as hydrocephalus congenitus, osteogenesis imperfecta, metopism, *Luckenschadel* (Wieland), *Weichschadel* and *Reliefschadel* (M B Schmidt), dysostosis cleidocranialis, the vast group of manifestations of status dysraphicus (including spina bifida, syringomyelia, hydromyelia, encephalocele and myelocele), heterochromia of the iris (Hess³), cryptorchism (Hess⁴¹) and Sprengel's deformity associated with defects of the spine (Dutoit⁴²) All these conditions are to be considered not as localized and confined to a small area, but as representing widespread involvement of the skull or of the entire skeleton They are based on a metabolic disorder, consisting of an anomaly of the ossifying process In none of these conditions has primary atrophy of the optic nerve been found, in spite of hydrocephalus This confirms the statement that the primary atrophy in the group of diseases discussed is due to a limited congenital anomaly The date of the beginning of this anomaly may be about the third month of embryonic life

Functional Signs—These may be interpreted as dependent on a disturbed function of the pituitary-diencephalic system They exhibit a striking similarity to the signs noted by Karplus and Kreidl¹⁹ and Ranson²⁰ after stimulation of the vegetative center on the floor of the brain, in the diencephalic area close to the chiasm

The atrophy of the optic nerve under discussion is not of inflammatory origin; neither are the signs of acute glaucoma The course of the atrophy is progressive and irretrievable, as congenital anomalies of the central nervous system commonly are It is not primarily associated with nystagmus The latter, if present, is due to impairment of eyesight This fact may be explained by the lack of connection of labyrinthine nystagmus with the forebrain *The triad—optic nerve atrophy, structural anomalies of the middle fossa and diencephalic signs—may throw light on the pathogenesis of atrophy of the optic nerve* in certain congenital and in some acquired organic diseases, as will be shown in the fifth article of this series The origin of this atrophy has been veiled in complete darkness Deeper and more extensive studies are required to substantiate this view It may, nevertheless, be recalled that in the second article⁹ evidence was provided for the intervention of the diencephalic area in the pathogenesis of glaucoma The main clinical signs of glaucoma could be traced back to a nervous factor originating in this area In the present article, various suggestions are made that a certain type of atrophy of the optic nerve may originate in the same locality

15 Kenwood Street, Brookline (46)

40 Hess, L Human Biol 18:61, 1946

41 Hess, L J Nerv & Ment Dis 97 423, 1943

42 Dutoit, F Brain 54 421, 1931

SENSORIAL RETINAL RELATIONSHIP IN CONCOMITANT STRABISMUS

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I. INTRODUCTION

CORRESPONDING RETINAL ELEMENTS

NORMAL AND ANOMALOUS RETINAL CORRESPONDENCE

ALL VITAL manifestations in man have an objective and a subjective aspect. The interrelation of these two aspects represents one of the most complex problems of psychophysiology and philosophy. But the relation is accessible to a relatively simple analytic investigation when it is reduced to the basic sensory phenomena, as, for instance, in studying the act of vision. Such studies do not require the solution of the general problem—if this is at all soluble by rational methods—but, rather, form the basis for it.

In the act of vision the "objective sphere," or "aspect," consists in (a) the object points in space and the wavelengths emitted or reflected by them (visual stimuli) and (b) the geometric optic properties of the refractive media of the eye, which determine the place and character of the dioptric image on the retina, and, furthermore, (c) the anatomic and physiologic properties of both the structures sensitive to light in the eye and the nerve pathways and centers involved (peripheral and central part of the visual apparatus). The "subjective sphere" is represented by the perception of light, color and form and by the subjective localization of objects.

The visual apparatus is not a receptor organ in a purely passive sense; it is an instrument which actively transforms the objective world of visual stimuli into man's subjective world of color, form and spatial distribution.

It would eliminate confusion in the terminology of physiologic optics if consistent distinction were made between the subjective and the objective sphere in the act of vision. But such a distinction exists only in part. It is obvious to any one that the terms wavelength and color are not interchangeable, but in the field of space sense there is no

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unequivocal terminological differentiation between the objective and the subjective visual space¹

It is, therefore, doubly necessary to achieve a clear understanding of the fact that the objective and subjective spheres are incommensurate. There is no yardstick for the subjective sphere, and the measurements which one is able to make in the objective sphere are not directly applicable to the subjective sphere. However, there is a constant relation between the two, and, although its exact nature is not known, the fact that this constant relation exists makes it possible to characterize quantitatively man's subjective world by observing the changes which it undergoes under the influence of measurable changes in the objective world²

In this way it has been established that there are certain constant discrepancies between the objective and the subjective visual space. It is known, for instance, that a plumb line seen monocularly to the exclusion of all other visual objects in the field of view appears to most observers to be tipped templeward with its upper end. It is known, furthermore, that all observers make a constant error in attempting to divide a monocularly seen straight line when nothing but the line is visible to the observer (Kundt-Munsterberg partition experiment). These and other discrepancies are due to a peculiar distribution of the retinal elements, or, rather, their spatial values.

The difference between the objective and the subjective visual space is most vividly demonstrated when one examines the subjective localization in binocular vision. By simplifying the visual space for the purposes of the experiment and by excluding all accessory clues for spatial localization,³ it can easily be shown that the objective position of points

1 The good German writers make such a differentiation. They distinguish, for instance, between *Gesichtsraum*, *Gesichtsfeld*, *Aussenobjekt* or *Gesichtsobjekt*, *Fixationspunkt* and *Längshoropter*, on the one hand, and *Sehraum*, *Sehfeld*, *Sehding*, *Anschaungsbild*, *Kernstelle* and *Kernfläche*, on the other. The first group refers to the objective space, the second, to the subjective space. Tschermak-Seysenegg, A. *Optischer Raumsinn*, in Bethe, A., von Bergmann, G., Emden, G., and Ellinger, A. *Handbuch der normalen und pathologischen Physiologie*, Berlin, Julius Springer, 1931, vol. 12, pt. 2, p. 893.

2 Tschermak-Seysenegg, A. *Der exakte Subjektivismus in der neueren Sinnesphysiologie*, *Arch. f. d. ges. Physiol.* **188** 1, 1921.

3 Physiologic, as well as clinical, experience has shown beyond any doubt that the basis of binocular vision—the identity of the visual direction of corresponding points and stereoscopic depth perception based on the simultaneous stimulation of horizontally disparate retinal elements—is an innate factor. There are, however, numerous ocular factors (such as all perspective clues and form clues), as well as extraocular ones (such as tactile and proprioceptive clues derived from the position and movement of the body), which materially influence spatial orientation under ordinary conditions of seeing. These factors are sum-

in space does not coincide with the localization which is subjectively attributed to them

Assume that a normal subject fixates binocularly the object point F and that there are two other object points, A_L and A_R , in his field of view (fig 1 A). Suitable screens are so arranged that he sees A_L only with the left eye and A_R only with the right eye. As long as the subject continues to fixate F , he will see the object points A_L and A_R behind each other in the direction indicated by the arrow ϕ . Analogously, the object points B_L and B_R (fig 1 B) will appear behind each other in the direc-

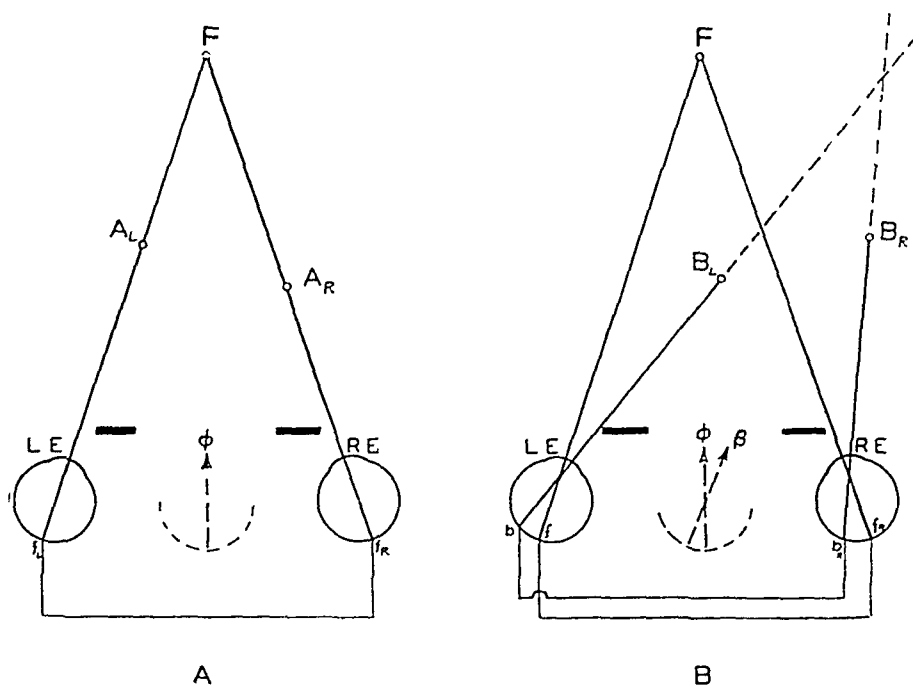


Fig 1—The lines of direction and the visual directions Ff_L and Ff_R are lines of direction of the foveae f_L and f_R , B_Lb_L and B_Rb_R , lines of direction of the retinal elements b_L and b_R , ϕ and β , common visual directions of the foveae f_L and f_R and the retinal elements b_L and b_R . In A, the object points F , A_L and A_R appear to lie behind each other in the direction ϕ , in B, the points B_L and B_R behind each other in the direction β .

tion β as long as the subject fixates the point F , which continues to appear in the direction ϕ . Thus, the subjective localization of the points A_L , A_R , B_L and B_R is at variance with their objective position. The

marized under the heading of "empiric factors of spatial orientation," since they are acquired through experience in the subject's life. The latter factors generally have to be excluded in experiments concerned with binocular spatial localization. The relationship between the two groups of factors is discussed by H. M. Burian (Influence of Prolonged Wearing of Meridional Size Lenses on Spatial Localization, *Arch Ophth* 30:645 [Nov] 1943). See also Tschermak-Seysenegg¹ and Fleischer, E. Die Querdissparation als physiologische Grundlage des binokularen Tiefensehens, *Ztschr f Psychol* 47:65, 1939).

pairs of points indicated by the same letter appear to lie in the same direction, although they are widely separated in space. How can this discrepancy be explained?

The lines which connect in a geometric construction the object points with the retinal elements on which they are imaged are called the "lines of direction." Their position is determined by the geometric optical properties of the media through which the rays of light emitted or reflected by the object points pass before reaching the sensory epithelium of the retina. The lines of direction belong to the objective sphere, and they determine only which retinal element will be stimulated by the object point. The position or localization of the subjective correlative of that point in the subjective space, that is, where it will be seen, is determined by another, a subjective factor, designated as the "spatial value" of the stimulated retinal element.⁴ This spatial value manifests itself in the direction in which the point appears in subjective space, each retinal element possesses a certain "visual direction," in which the stimulus which reaches the retinal element is localized. The objective lines of direction thus have their subjective correlative in the visual direction.⁵

The line of direction which connects the fixation point with the fovea is of special importance. It is the "principal line of direction," the "visual line" or "the line of gaze."⁶ The visual direction of the fovea is also of particular significance, it is the "principal visual direction." It must be emphasized that the visual directions are not absolute directions, they change with the position of the eye, but their relation to the principal visual direction remains the same.

The spatial values are inherent in each retinal element, owing to the anatomically fixed nervous connections with the cortex of the brain, in which all elements of the retinal mosaic are represented in analogous distribution.⁷ But the directional spatial values make sense only so far

4 The terms "retinal element" and "retinal point" are used throughout this article in the sense defined by C. S. Sherrington (*The Integrative Action of the Nervous System*, New Haven, Conn., Yale University Press, 1906, p. 377) as "the retinocerebral apparatus engaged in elaborating a sensation in response to excitation of a unit area of retinal surface." Similarly, "retina" is the integral of these unit areas.

5 The two are not synonymous, and the visual directions as such are independent of the lines of direction. This is evidenced by the fact that localized mechanical or electrical stimulation of retinal elements causes the appearance of a phosphen in the very same direction in which an object causing optical stimulation of the same retinal elements would be localized. In the case of mechanical or electrical stimulation, there are, of course, no lines of direction.

6 With regard to this terminology, see Lancaster, W. B. *Terminology in Ocular Motility and Allied Subjects*, *Am. J. Ophth.* **26** 122, 1943.

7 Certain restrictions applying to this statement will be made later.

as they are related to the visual direction of the fovea. They are, therefore, designated as "relative directional spatial values."

In figure 1, the lines of direction are indicated by solid lines, the visual directions, by arrows. Ff_L and Ff_R are the lines of direction of the foveas, B_Lb_L and B_Rb_R , the lines of direction of the retinal elements b_L and b_R . ϕ is the visual direction of the foveas, and since A_L and A_R are also situated on the lines of direction of the foveas and therefore imaged on them, they are subjectively localized in the principal (foveal) direction. Similar considerations apply to the subjective directional localization of the object points B_L and B_R , which have the same relative distribution⁸ and stimulate the retinal elements b_L and b_R . The subjective direction in which the object points A_L , A_R , B_L , B_R appear is determined by the relative directional spatial values inherent in the retinal elements.

It is evident from figure 1 that certain elements of the two retinas have one and the same spatial value or visual direction. The points A_L and A_R will appear in the same subjective direction, ϕ , no matter whether they are objectively situated on the visual line of the left or of the right eye, and a similar deduction applies to all other points in space. This fact is the most basic principle in the physiology of binocular vision and is known as the "law of the common visual direction."⁹

The retinal elements which have common visual directions are "corresponding retinal elements." This is the only adequate definition of corresponding retinal elements¹⁰ and satisfies all needs. It can also be

8 The lines of direction pertaining to the points B_L and B_R subtend the same angles at the nodal point of the left and the right eye, respectively.

9 Hering, E. (a) *Zur Lehre vom Ortssinn der Netzhaut, Beiträge zur Physiologie*, Leipzig, Wilhelm Engelmann, 1861, book 1, (b) *Das Gesetz der identischen Sehrichtungen*, *Arch f Anat, Physiol u wissenschaftl Med*, 1864, p 27, (c) *Der Raumsinn und die Bewegungen des Auges*, in von Hermann, L. *Handbuch der Physiologie*, Leipzig, F C W Vogel, 1879, vol 3, chap 5 (d) Hillebrand, F. *Die Heterophorie und das Gesetz der identischen Sehrichtungen*, *Ztschr f Psychol u Physiol d Sinnesorg* 54 1, 1909 (e) Tschermak-Seysenegg.¹

10 The concept of corresponding retinal elements has caused a great deal of confusion. F H Verhoeff (*Anomalous Projection and Other Visual Phenomena Associated with Strabismus*, *Arch Ophth* 19 663 [May] 1938) stressed this and offered a new definition of corresponding retinal points. I find myself in disagreement both with the basic assumption and with many details of Verhoeff's paper and feel that, in view of the great authority which every article by this distinguished writer carries, a documented dissenting opinion should be voiced for the benefit of those who are less acquainted with the subject.

However, since this paper is not primarily a controversial one, but intends to bring a constructive contribution to the knowledge of the sensorial retinal relationship in pathologic conditions, the discussion of Verhoeff's views will be postponed until the end of this paper.

formulated in the following way Corresponding retinal elements are those elements of the two retinas the stimulation of which, in binocular vision, gives rise to the localization in one and the same visual direction, no matter whether the stimulus reaches the retinal elements in one eye alone or the corresponding elements in the other eye alone or both simultaneously

For certain purposes it is expedient to add other characteristics to the definition of corresponding retinal elements, such as their distribution If one performs a mental experiment and superimposes the right on the left retina so that the two foveas and the principal meridians coincide, a pin stuck into any part of the retinas which cover each other will strike corresponding retinal elements Generally speaking, corresponding retinal elements have the same relative position with respect to the fovea¹¹ However, this is only a secondary property of the corresponding retinal elements, it is not essential and only approximately true

Neither should the definition be based on the fact that the simultaneous stimulation of corresponding retinal elements conveys a single visual impression The corresponding points share this property to some extent with the so-called noncorresponding, or disparate, retinal elements¹² The only quality which is proper to the corresponding retinal elements, and only to them, is the common visual direction

It is a consequence of the existence of corresponding retinal elements that the two eyes of a normal person must be considered a single organ from a subjective sensorial point of view The imaginary third eye shown in figure 1, which contains the visual directions of the corresponding retinal elements and their intersection,¹³ represents this

11 von Helmholtz, H Helmholtz's Treatise on Physiological Optics, edited by J P C Southall, Ithaca, N Y, The Optical Society of America, 1925, vol 3, p 417 It is assumed in this gross mental experiment that the spatial values are uniformly distributed in the two retinas This is not the case, and the position of the corresponding points can be determined only by subjective criteria (cf Hofmann, F B Die Lehre vom Raumsinn, in Graefe, A, and Saemisch, T Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1925, vol 3, pt 2, chap 13, p 218)

12 A single visual impression is obtained also by simultaneous stimulation of noncorresponding retinal elements which lie within the so-called Panum areas, and stereoscopic single vision is possible altogether only on the basis of simultaneous stimulation of horizontally disparate retinal elements

13 Experiment has shown that the center of the visual directions is not always in the median plane of the observer's head, it may be shifted toward one eye or the other This was already known to Hering, and it is unquestionably of a certain practical importance but is not of further concern in this paper However, it is of interest to note it here in passing, because in the case of a shift of the center of the visual directions toward one eye or the other, not even the fixation point *F* would coincide with its subjective correlative (the *Kernstelle*, in Hering's terminology)

"cyclopean eye," which is the subjective correlative of the two objective eyes. But it must always be borne in mind that both the visual directions and "the cyclopean eye" are nothing but the description of a subjective experience.¹⁴

It has been emphasized that the visual directions represent relative spatial values. The secondary visual directions have a fixed position only relative to the principal visual direction. The principal visual direction has no absolute position relative to the coordinates of the subjective space or to the subjective coordinates of the observer's head. The absolute position of the principal visual line changes with the position of the eyes. The "absolute," or "egocentric, spatial localization," which is clinically investigated, for instance, by the pointing experiment in cases of paralyzes of the ocular muscles, must be clearly distinguished from the relative spatial localization. It will be seen in later sections of this paper that much of the confusion existing in the literature on anomalous retinal correspondence is caused by the fact that this distinction is not clearly understood.

In defining corresponding retinal elements, one has at the same time defined "normal retinal correspondence", one has only to change the wording and to state that the sensorial retinal relationship, or the retinal correspondence, is normal if the retinal elements which should be corresponding, such as the two foveas, have common visual directions.¹⁵ From this definition of normal retinal correspondence one can derive logically a definition of "anomalous retinal correspondence." If elements of the two retinas which are *de norma* noncorresponding or disparate—for instance, the fovea of one eye and an eccentric retinal element of the other eye—acquire a common visual direction, this new sensorial relationship is termed anomalous.

14 Hofmann, on page 236 of his monograph,¹¹ expressed this idea clearly in the following passage: "The fact must be emphasized that the theory of the visual directions is not to be understood as though the retinal images were 'projected outward' from the median imaginary eye along the visual directions instead of from each individual eye along the lines of direction. This opinion, like the projection theory in general, is derived from the false assumption that the retinal images are first presented to the mind and that subsequently one must somehow have transposed them into space. Indeed, most people have no inkling of their existence but are aware only of the sensation in the subjective visual space. The visual directions are only a subsequent intellectual reconstruction of this immediate experience."

15 The definition of normal correspondence requires, however, the added qualification that the simultaneous stimulation of the corresponding retinal elements must convey a single visual impression which is not accessible to further analysis. This was pointed out in a previous paper (Burian, H. M. Fusional Movements in Permanent Strabismus. A Study of the Role of the Central and Peripheral Retinal Regions in the Act of Binocular Vision in Squint, Arch. Ophth. 26:626 [Oct.] 1941).

Before showing that the condition of anomalous retinal correspondence is not merely a logical deduction and that the definition given is supported amply by clinical evidence, one must first review the methods in use for the clinical determination of the sensorial retinal relationship. It is of importance for the interpretation of the results to have a thorough understanding of these methods, because, as will be seen later, the results of the examination depend largely on the conditions under which the examination is performed.

II METHODS USED IN THE CLINICAL DETERMINATION OF THE SENSORIAL RETINAL RELATIONSHIP

Ingenuous laboratory methods have been devised for the determination of the distribution of corresponding elements in the retinas of normal persons. These methods, however, are not applied routinely in clinical examinations and are not of concern in this paper.

The methods employed for the clinical determination of the retinal correspondence can be divided into two groups. The first group comprises the methods in which the objective position of the eyes, the angle of squint, is compared (*a*) with the subjective directional localization of a biretinal stimulation or (*b*) with the angle at which the patient superimposes or fuses dissimilar visual impressions reaching the two retinas. In the second group the subjective visual direction, or directions, of the two foveas are determined directly. These methods will now be discussed in some detail.

1 METHODS COMPARING THE POSITION OF THE EYES WITH THE SUBJECTIVE LOCALIZATION

Double Image Test—The images of all object points seen through a prism are shifted on the retina in the direction of the base of the prism. Assume that a prism too strong to cause fusional movements is placed with the base nasalward in front of the right eye of an observer who at first fixates binocularly the object point *F* (fig 2A). The image of the fixation point *F*, which previous to the introduction of the prism impinged on the right fovea f_R , is now shifted to the nasal retinal point l_R ; there is an object point *P*, which was originally imaged on the temporal retinal element p_R and is now imaged on the fovea f_R . However, no change has occurred in the position of the images of the left eye, the fixation point *F* is still imaged on the fovea f_L , and the object point *P*, on the nasal retinal element p_L . Nor has the sensorial retinal relationship been altered by the introduction of the prism, and the law of the common visual directions still applies. Therefore, since *F* is imaged on the left fovea and *P* on the right fovea, both points must appear in the visual direction ϕ of the foveas. On the other hand, the fixation point *F* is imaged on the fovea of the left retina and on an eccentric element

of the right retina. These elements of the two retinas are disparate and thus have different visual directions. Therefore, the point F must be localized in two directions in the subjective space. Analogous deductions apply to all other object points, none of them is imaged on corresponding points, and consequently they must all be represented by two sensations in the subjective space, indeed, all object points seen by the observer will appear to him to be double.

If the observer pays close attention to the double images, or if the stimuli reaching the two eyes are in some way differentiated, it will be possible for the observer to give exact information as to the position and distance of the double images. If the prism is placed with its base nasalward, as shown in figure 2 A, the double images will be displaced toward the eye which has the prism in front of it. This condition is

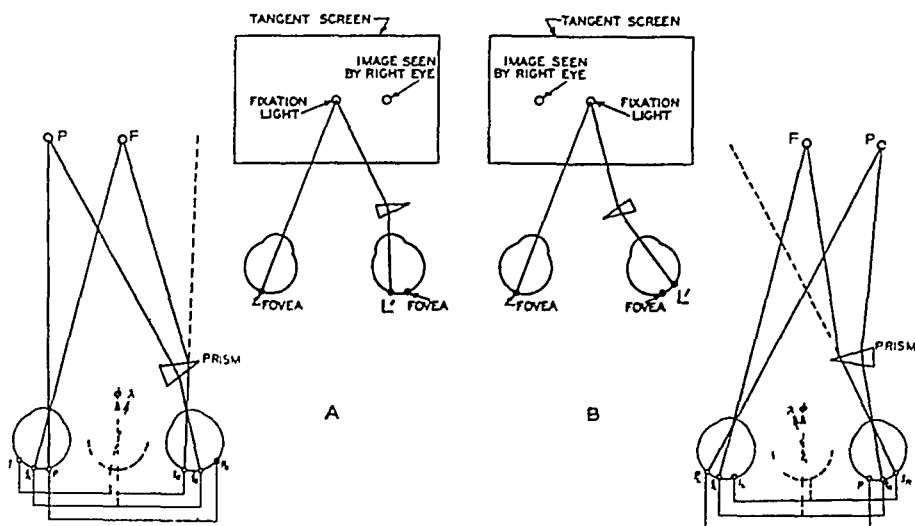


Fig 2—Diplopia produced by prisms. *A*, prisms with base placed nasalward in front of the right eye (uncrossed diplopia), *B*, prism with base templeward in front of the right eye (crossed diplopia)

designated as “homonymous, or uncrossed, diplopia.” If a prism with its base templeward is introduced in front of one eye (fig 2 *B*), the fixation point, together with all other object points, is shifted toward the temporal side in that eye. The condition thus created is in every respect analogous to the one which is produced by the introduction of a prism with the base in the nasal direction, but the sign is opposite. The double images are displaced in the direction of the contralateral eye, i.e., a “heteronymous, or crossed, diplopia” will occur.

In addition to the position of the double images, their separation from each other is also characteristic. The relation of the common visual directions of the eccentric retinal elements to the visual direction of the foveas is a quantitative one. If the strength of the prism chosen for the experiment is such that it displaces the images in one eye 10

arc degrees, the double images will appear to be 10 arc degrees apart. In other words, the distance of the double images, measured in arc degrees or prism diopters, is equal to the strength of the prism, the distance of the double images is a measure of the introduced prism strength.

This is true not only for prisms placed horizontally in front of an eye, but also for those placed in a vertical position. The double images will appear above and below each other, and their angular separation is always equal to the prism strength.

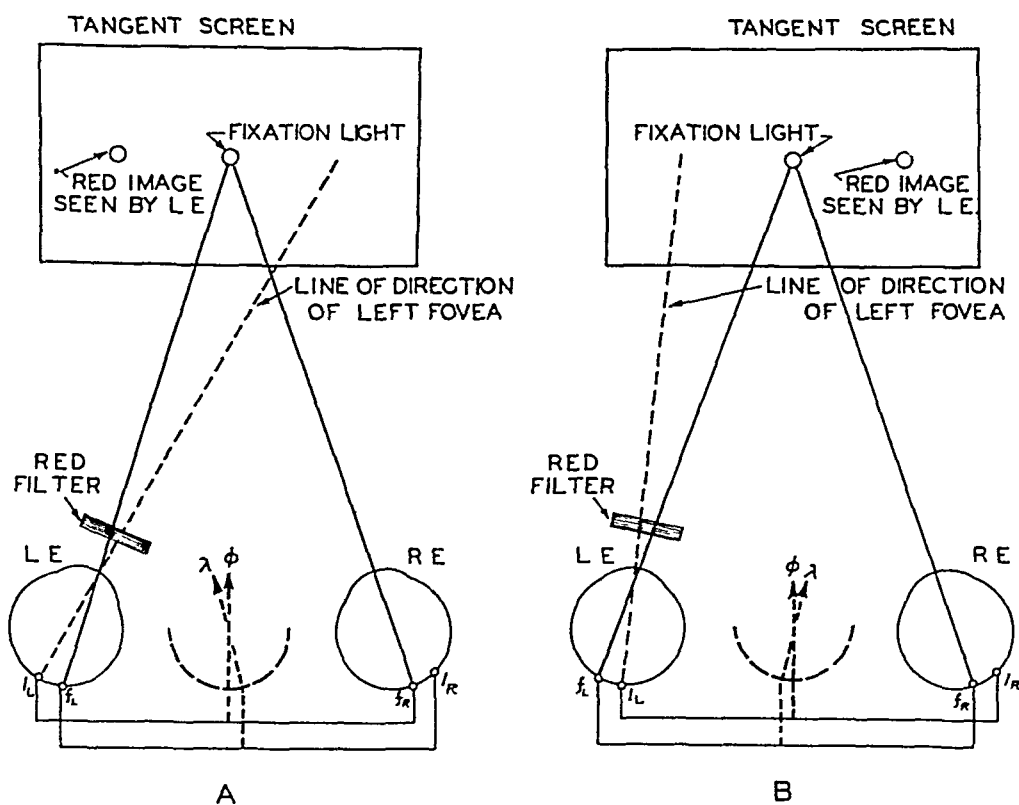


Fig 3—Diplopia in strabismus with normal correspondence A, uncrossed diplopia in convergent strabismus, B, crossed diplopia in divergent strabismus

A patient with convergent or divergent strabismus whose retinal relationship is normal reacts in no way differently from the normal observer who has a horizontal prism in front of one eye except that he is usually not aware of diplopia because of suppression. Assume that the left eye is turned in 10 arc degrees when the right eye fixates the object point F (fig 3 A). The image of the fixation point then falls on an eccentric nasal point of the left retina, the distance of which from the fovea is 10 arc degrees. The result is that point F appears in two directions in the subjective space, namely, in the directions of ϕ and λ . The angular separation of the double images is 10 arc degrees, and the image seen with the left eye is to the left of the one seen by the right eye (uncrossed diplopia).

If the patient has a divergent strabismus of 10 arc degrees in the left eye (fig 3B), object point *F* appears in the subjective visual directions ϕ and λ , and the double images are again separated by 10 arc degrees, but this time the image seen by the left eye is to the right of that seen by the right eye (crossed diplopia)

When the retinal correspondence of a squinting patient is disturbed, he will no longer localize the double images as would a normal observer who has a prism in front of one eye. The distance of the double images, as seen by the patient, will be smaller than would be expected from the objective determination of the angle of squint, and he may even show heteronymous, instead of homonymous, diplopia and vice versa

Normally, the two foveas have one and the same visual direction. In anomalous correspondence the visual directions of the deviated eye are shifted in such a way—relative to the visual directions of the fixating eye—that the fovea of that eye has a common visual direction with an eccentric retinal element of the other eye. Thus the two foveas now have two visual directions and the angle between the two is called the “angle of anomaly,” or “angle of adaptation” (Chavasse). This angle is indirectly determined in the double image test and on the synoptophore, or directly in Lancaster’s red-green test, or in a more perfect way in the after-image test.

By comparing the objectively measured angle of squint with the angular distance of the double images, one can form a judgment about the sensorial retinal relationship in a patient with strabismus. If the angle of squint is 10 arc degrees and the double images have an angular distance of 10 arc degrees, the angle of anomaly is zero, and the retinal correspondence is normal. If the angle of squint is 10 arc degrees and the double images coincide (angular distance, zero), the angle of anomaly is also 10 arc degrees, and there is anomalous correspondence adapted to the angle of squint. If the angle of squint is 10 arc degrees but the angular distance of the double images is only 5 arc degrees (angle of anomaly, 5 arc degrees) then there is an anomalous correspondence which is not adapted to the angle of squint¹⁶

16 Tschermak-Seysenegg¹ has divided on this basis all patients with concomitant squint into the following three groups: group I patients who have a motor anomaly (strabismus) but whose sensorial relationship is normal, group II patients with a motor anomaly and a harmonious (fully adapted) sensorial anomaly, group III patients with a motor anomaly and a nonharmonious (subharmonious, Chavasse) sensorial anomaly. This classification is convenient and is recommended for general use. It is obvious that a patient may not at all times belong to the same category. He may have originally belonged to group II or III but may have been changed to group I by orthoptic treatment. Or he may have belonged to group II and have been operated on, immediately after the operation he may belong to group III.

Many different possibilities of anomalous localization of the double images do actually occur. I shall describe now only one instructive example, to which considerable attention will be given in a subsequent part of this paper. This is the case in which the angle of anomaly is equal to the angle of squint, i.e., the case in which the retinal correspondence is fully adapted to the angle of squint. If a patient has a convergent strabismus of the right eye of 15 arc degrees (fig 4 *A*), one expects to find that he will see uncrossed a double image the angular separation of which is 15 arc degrees. However, on examination, one may find that the patient does not see double and that the two differentiated images of the fixation point *F* coincide in his subjective space, although the right eye is deviated. What has happened? The two foveas no longer have a visual direction in common. The sensorial

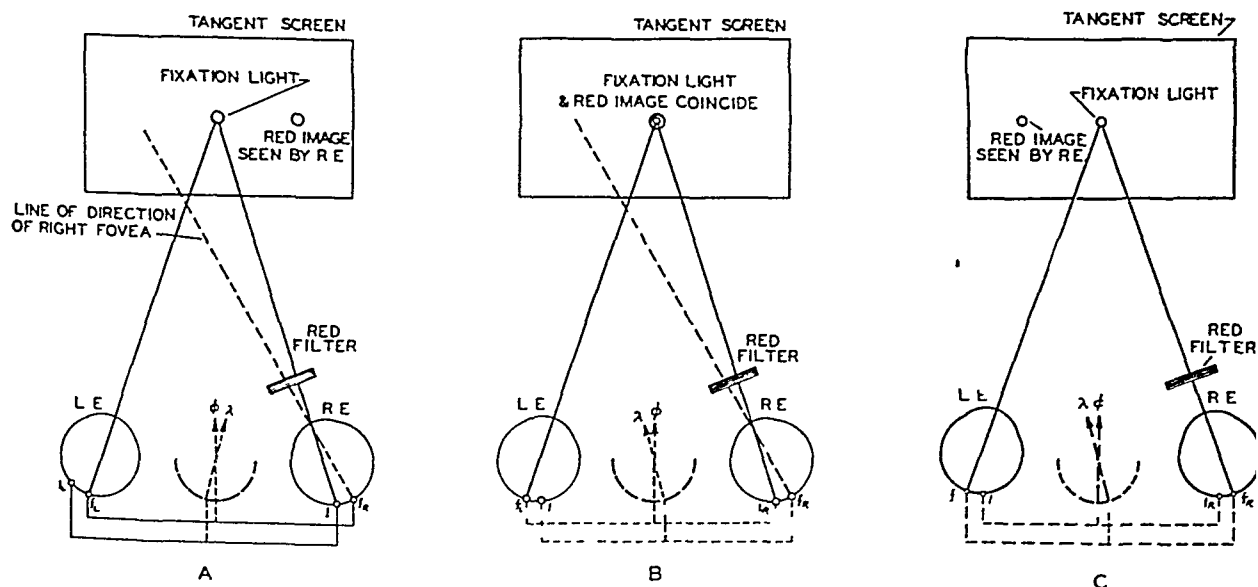


Fig 4—Convergent strabismus of the right eye *A*, uncrossed diplopia in normal correspondence, *B*, no diplopia in harmonious anomalous correspondence, *C*, postoperative crossed diplopia due to persistence of anomalous retinal correspondence

relationship of the two retinas has adapted itself to the altered mechanical conditions, and the fovea of the left eye has acquired a common visual direction with that of the eccentric point l_R , situated 15 arc degrees to the nasal side of the right fovea (fig 4 *B*). These disparate elements of the two retinas now have an anomalous common visual direction, and the object points *F* and *P* are therefore localized in the common visual direction ϕ in the subjective space. The angle of anomaly (i.e., the angle between the visual directions of the two foveas) is 15 arc degrees.

If the patient were operated on and the angle of squint were reduced to zero, the patient would at first—and often for a long time after the operation—retain his sensorial anomaly, that is to say he would still

show an angle of 15 degrees between the visual directions of the two foveas. As a result, he would then show diplopia in the double image test, although the visual lines of the two eyes intersect at the fixation point. The double image would be localized in a crossed position, at an angular distance of 15 arc degrees from the fixation light (fig 4 C).¹⁷

The practical application of the double image test is simple, and the test can be performed with means easily accessible to every ophthalmologist. All one needs is a tangent scale or tangent screen with a light in its center and a loose red filter or a Maddox rod. The test is performed in a lighted room, in order to permit observation of the patient's eyes.

After the patient's angle of squint has been objectively determined, he is seated at a suitable distance (not less than 2.5 meters) in front of the center of the tangent scale and is asked to fixate the light. A red filter is then placed in front of one of the patient's eyes. The other eye sees the yellow fixation light and the numbers on the tangent scale, as a rule this eye is used for fixation. A patient who has strabismus, or for that matter heterophoria, now usually sees two lights, a red one and a yellow one, and he is asked whether the red light is to the left or to the right, whether it is above, below or on a level with the yellow light and near which number or numbers it is located. Knowing the type and amount of the patient's strabismus, one also knows what answer one must expect if his retinal correspondence is normal. If the answer differs from the one expected, the patient's retinal correspondence is usually anomalous.

The test can be performed successfully on children of average intelligence as young as 3 years of age. But for all its simplicity of execution, the double image test requires a certain amount of experience if errors are to be avoided and if difficulties, which arise frequently, are to be overcome.

The red filter must be sufficiently dark to eliminate from the field of view everything except the fixation light, which appears as a red spot. This is essential, the double image test is designed on the basis of complete dissociation of the two eyes, and this is not achieved if the covered eye can faintly see the scale or other objects through the filter.

The test is facilitated greatly if it is begun by covering alternately first one eye of the patient and then the other, showing him that he sees with one eye the fixation light and the scale and with the other a red spot of light. Then, when both eyes are uncovered, the patient is more likely to be aware of the double images. It is frequently difficult to elicit double images in testing patients with strabismus because of their

¹⁷ This postoperative crossed diplopia was observed early in the study of cases of strabismus and was designated as paradoxical diplopia.

tendency to suppress the images of the deviated eye, especially in the presence of pronounced amblyopia. However, it is almost always possible to make the patient conscious of the double images if the test is applied with sufficient patience and some skill. One should never be satisfied with a double image test in which only one eye is covered by the red filter. One should always attempt to perform the test by covering first one eye and then the other and comparing the answers received. These answers are not always identical. Frequently one finds a so-called "dissociated vertical divergence" combined with a strabismus¹⁸. This condition is characterized by an upward movement of the covered, darkened eye and is expressed in the double image test in the apparently contradictory finding that there seems to be a right hyperphoria when the right eye is covered and a left hyperphoria when the left eye is covered. A small dissociated vertical divergence often escapes notice in the cover test, and the only certain way in which it can be detected is by a properly executed double image test. Another reason for covering the two eyes alternately with the red filter is the interesting fact that the retinal correspondence may vary according to which eye is used for fixation, this will be discussed in more detail in a later part of this paper. Finally, if the double image test is used in a case of recent paralytic strabismus, the difference in localization when the eyes are covered alternately is an indication of the difference between the primary and the secondary angle of squint.

In making the double image test, the red glass should always be placed first in front of the eye which the patient uses habitually for fixation. In virtually all cases of strabismus there is some degree of suppression, by dimming first the image of the dominant eye, it is easier to elicit double images and to teach the patient what he is supposed to see. Even when this precaution is used, it is not always possible to obtain double images. One frequently has to resort to a simple device which never fails in the end to give the desired result. By placing together with the red filter a prism of 5, 10 or 15^Δ base up or base down in front of one eye, the image is displaced to a peripheral region where the suppression is not very strong. The patient will immediately and precisely report the position of the double image. In evaluating the result of the test, the fact that a prism was introduced must, of course, be taken into account.

If one eye is highly amblyopic, the patient may be unable to perceive the faint red image of the fixation light as seen through the filter. In such cases one has either to choose a lighter red filter or be satisfied

18 Bielschowsky, A. Disturbances of the Vertical Motor Muscles of the Eyes, *Arch Ophth* 20 175 (Aug) 1938

with the result obtained in the first half of the test, when the normal eye was covered

Another difficulty which may occasionally arise is due to the inability of patients with anomalous correspondence to localize the position of the double image relative to the central light of the scale. They see both lights and see them simultaneously, but they are unable to tell anything about the localization of the double image, they may not even be able to state whether the red light is to the right or to the left of the white light or whether they are 2 feet or 1 inch (60 or 25 cm) apart. This happens only when the retinal correspondence is anomalous, theoretically, cases of this kind are of importance and will be discussed later. Practically, one may be satisfied with the statement that the patient shows anomalous correspondence in the double image test. If a quantitative determination of the angle of anomaly is desired, it can in the end be obtained even in these cases if the examiner has sufficient patience and repeats the test often enough. Vertical prisms are again helpful, just as in the presence of marked suppression.

It is always necessary to make sure by questioning the patient whether or not he sees the two lights simultaneously. Certain patients have a capacity for very rapid alternation and may report that the red and the white light coincide, from which one would conclude that there is an anomalous correspondence adapted to the angle of squint. Unless one has made sure that the patient sees the two lights simultaneously, one cannot rely on this conclusion.

Even when it seems beyond doubt that the patient's reports are reliable, it is often advisable to verify the findings by adding prisms successively in the four cardinal directions and to check the patient's answers by the prism displacement. This is useful when one is examining small children. Such children, especially those of preschool age, should not be asked to tell where they see the red light, but should be invited to go to the scale and put their finger on the place where they saw the red light.

Prisms must also be used in the double image test to offset part of the angle of squint if the angle is very large. But it is not advisable to correct the angle fully. In this event there would be a simultaneous stimulation of both foveas, and this results at times in a different localization than when one fovea and a peripheral element of the retina of the other eye are stimulated,¹⁹ which is the way in which the eyes of a

19 Burian¹⁵ Since publishing this paper, I have found that von Graefe made the same observation as early as 1855. He reported it in his masterly way and interpreted it correctly (von Graefe, A. Ueber eigenthumliche, zur Zeit noch unerklärliche Anomalien in der Projektion der Netzhautbilder, Arch f Ophth 1 284, 1855). A man with a small residue of convergent strabismus after operation

squinting patient are used under normal conditions. However, if it is desired to investigate the response of the two foveas to simultaneous stimulation, for instance, previous to operation, this can easily be done by reducing the angle of squint to zero with the help of prisms and repeating the double image test.

This test reveals whether a patient uses normal or anomalous retinal correspondence, but it also offers an opportunity for a quantitative determination of the angle of anomaly. One must, however, recognize the fact that the accuracy of the method is limited by the relatively low degree of accuracy inherent in all measurements for strabismus. The angle of squint is subject to fluctuations and may vary while the double image test is performed. One would, therefore, not be justified in saying that a patient has anomalous correspondence because the angle of squint measured objectively was 16 arc degrees and the angle of anomaly was 14 arc degrees. These differences will naturally be less apparent if the angle of squint is large, but they may become very noticeable if the angle of squint is small. If the discrepancies are considerable, it is advisable to redetermine the angle of squint objectively.

In general—and this applies to all objective and subjective tests for strabismus—one should never satisfy oneself with a single test. Each test should be repeated two or three times successively and rechecked at different times. Only thus can one obtain reliable information about the motor and sensorial conditions in a case of strabismus. Not only is the angle of squint subject to certain changes, the anomaly of the retinal correspondence is by no means a fixed and unchangeable one. To be sure, in some instances it is deeply rooted and remains exactly the same over a period of years of observation. In others it is not so firmly established and is then subject to frequent changes. To ascertain this fact is in itself of importance for the prognosis in the individual case.

Modifications of the Double Image Test—Modifications of the double image test have been devised. One of them is Lancaster's red-green test²⁰. In this test there is no central fixation light on the tangent screen. The patient wears red-green spectacles—red on the right eye and green on the left eye. With a red and a green flashlight projector, red or green spots or lines can be thrown on any desired place on the screen. If the patient is to fixate with the right eye, the examiner handles the red projector, and the patient handles the green projector, if the patient is to fixate with the left eye, patient and examiner exchange

showed slightly uncrossed diplopia when fixating with that eye. When the angle of squint was compensated for by prisms, there suddenly was crossed diplopia with considerable distance between the double images. No change in the position of the eyes accompanied the sensorial change.

20 Lancaster, W. B. Detecting, Measuring, Plotting and Interpreting Ocular Deviations, Arch Ophth. 22 867 (Nov.) 1939.

flashlights The examiner throws the red or green light on the chosen place on the screen, and the patient moves his flashlight until the red and green lights appear to him to be superimposed on the tangent screen From the objective position of the lights on the screen—and knowing the objective position of the patient's eyes—the examiner can conclude what his retinal correspondence is

The basic difference between the double image test as previously described and the red-green test is that in the former only one stimulus is in the field of vision of the two eyes, while in the latter a stimulus is presented to each eye, in the double image test the patient has to localize the double images resulting from the simultaneous stimulation of one fovea and an eccentric element of the retina of the other eye, in the

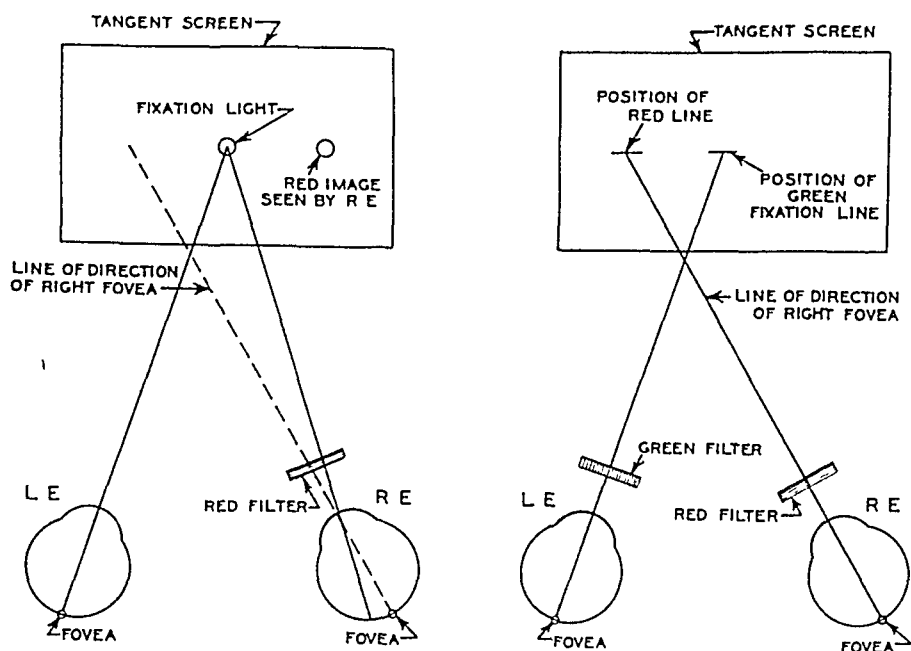


Fig 5—Diagrammatic comparison of the double image test with Lancaster's red-green test in a case of convergent strabismus of the right eye with normal retinal correspondence In the double image test, the fixation light is imaged on the fovea of the fixating eye and a peripheral element of the deviated eye, result uncrossed diplopia In Lancaster's test, each test line is brought onto the fovea of the eye with which it is seen, result crossed position of the test lines

red-green test the patient must superimpose subjectively the visual impressions reaching simultaneously the two foveas When this is achieved, the position of the lights on the screen indicates directly the lines of direction of the two foveas as long as the correspondence is normal Thus, the transposition of the findings, which is necessary in the double image test and which may appear tricky to the beginner, is avoided in the red-green test (fig 5) However, if the sensorial retinal relationship is anomalous, the position of the lights on the screen no

longer indicates the angle between the lines of direction of the foveas (the objective position of the eyes), but indicates the angle between the subjective visual directions of the two foveas (the subjective angle of anomaly)

The red-green test has one advantage over the double image test in the examination for concomitant strabismus, and that is its flexibility. If the examiner foregoes the advantage of avoiding the transposition and handles both projectors himself, he can stimulate simultaneously any desired part of the two retinas. He can then determine the retinal correspondence while stimulating the fovea of the fixating eye and an eccentric element of the deviated eye (both lights superimposed on the zero of the scale) or while stimulating both foveas (lights displaced on the screen according to the angle of squint), without resorting to the use of prisms. He must, however, constantly be on guard that the patient fixates with the eye with which he is supposed to fixate. This is rather difficult to do in the red-green test, as the goggles are large and the room is darkened.

This disadvantage does not exist in the projection arrangement which I described in a previous publication¹⁵. It allows the examiner to watch the patient's eyes constantly and has the same flexibility as the red-green test. Since projection lanterns are used, the examiner can, in addition to the behavior of the retinal correspondence, also study the binocular response of the eyes to various fusional stimuli, measure aniseikonia, and so on. This instrument was built for research purposes and does not pretend to be usable in routine practice. It will, therefore, not be discussed in this paper.

Travers²¹ has described a method which he called the mirror-screen test. In this test the patient is seated in the usual way in front of a Bjerrum screen. On one side of the patient there is another black screen, normal to the first, on which there is a movable light, seen by the patient in a mirror placed in front of the eye on the side of which is the second screen. A cover test is performed and the light placed in such a way that there is no movement of the eyes when fixating alternately the center of the Bjerrum screen and the light on the other screen. When both eyes are uncovered, the light will be seen by the patient in the center of the Bjerrum screen if his retinal correspondence is normal. If it is anomalous, the light and the center of the Bjerrum screen will not coincide, the distance between the two is a direct measure for the angle of anomaly. This test is also of interest mainly for research purposes.

21 Travers, T àB. Suppression of Vision in Squint and Its Association with Retinal Correspondence and Amblyopia, *Brit J Ophth* **22** 577, 1938.

Essence of the Double Image Test—Before other tests for determination of the retinal correspondence are discussed, the essence of the double image test must be summarized

In this test the attempt is made to determine the response of the patient to localized biretinal stimuli when the two eyes are dissociated. It is of importance to emphasize that small stimuli are used and that all fusional stimuli are purposely avoided. This permits the determination of the common visual directions of a restricted number of elements of the two retinas without the influence of extraneous factors. But it must be kept in mind that the result of the double image test is necessarily dependent on the position of the eyes, since this position determines which retinal elements are going to be stimulated. It will, therefore, change with a change in the angle of squint,²² whether it is spontaneous or is due to an operative procedure. One must be aware of this in order to interpret properly the results of the double image test.

The other factor in the evaluation of the double image test is that it does not attempt to duplicate the visual conditions present in the ordinary use of the eyes. When a person is using the eyes under ordinary conditions of seeing, there are always fusional stimuli and empiric clues reaching his two eyes, influencing his ocular performance even if there is a strabismus. Depending on the presence or absence of fusional stimuli and empiric clues, a difference in the response of the patient may be expected. Such clues and stimuli are present in the test for retinal correspondence with the synoptophore or with similar major amblyoscopes.

Determination of the Retinal Correspondence with the Synoptophore—The synoptophore, like all other major amblyoscopes, is a haploscopic arrangement consisting of two arms which pivot around a vertical axis situated exactly below the middle of the basal line of the patient's eyes. Various targets may be placed on the arms at a suitable distance from the center of rotation of the instrument, and the rays of light coming from the targets are directed, by means of prisms or other optical arrangements, in such a way that the image of the center of each target falls on the fovea of the right and the left eye of an orthophoric subject when the arms are parallel to the basal line. In that event, the subject's lines of gaze would also be parallel, since the optical system of the synoptophore is such that the targets are optically at infinity. If the observer is not orthophoric, what he sees will depend on the type of targets used. If the targets are similar, offering fusional, or even stereoscopic, stimuli, the observer will frequently be able to fuse the targets with parallel lines of gaze. If the targets are dis-

²² This distinguishes the double image test from the after-image test, as will be seen later.

similar, he may not be able to superimpose the images but will see one image higher or lower than, or to the right or the left of, the other, according to the nature of his heterophoria. By moving one or both arms of the synoptophore, the center of both targets can now be brought into such a position that the images of the centers fall on the foveas and the observer will see a single image. The position of the arms in which this is achieved can be read from scales, and the reading represents the heterophoria of the patient.

In examining a squinting patient with the synoptophore, one's first problem is, again, to determine the objective angle of squint, i. e. the angle between the lines of direction of the two foveas. This is done by placing the arms of the synoptophore into such a position that no movement of the eyes occurs when they assume alternately the fixation of their respective target. Once the arms are in that position, the patient should superimpose the dissimilar images used in the test if his retinal correspondence is normal. If the correspondence is anomalous, the patient will not see the images superimposed but will see them in a crossed or an uncrossed position, according to whether he has a convergent or divergent strabismus. By approaching the two arms to the zero position, the two images are brought closer until they are finally superimposed.

By presenting dissimilar targets to the patient in the synoptophore, it is attempted to dissociate the two eyes and to determine the visual directions of the foveas. There is, however, no reason that one should restrict oneself to dissimilar objects. Targets which are in part similar, or which may even contain stereoscopic stimuli, may also be used. In many instances there is a good deal of binocular cooperation between the eyes of a squinting patient, and by using various targets one will soon find that the reaction of some patients differs according to the target used in the test. Applied in this way, the synoptophore offers an opportunity to examine the eyes of a squinting patient under conditions which are comparable to the natural use of the eyes.

One must keep in mind that the task assigned to the patient is to superimpose stimuli which simultaneously reach the two foveas when the arms of the synoptophore are in the position of the "objective angle." When the arms of the instrument are in the position of the "subjective angle," one fovea and an eccentric element in the retina of the other eye are simultaneously stimulated. This is not always easy for the patient. The simultaneous stimulation of the two foveas is the thing which squinting patients try to avoid above all, suppression and changes in the angle of squint may make the test for retinal correspondence rather difficult. As I have pointed out,¹⁵ the patient's reaction may differ according to the location of the stimulus on the retina.

Comparison of Determinations of the Retinal Correspondence with the Double Image Test and with the Synoptophore—In the double image test, the eyes of the patient are completely dissociated, and a localized stimulus of light is allowed to fall on the fovea of one eye and on an eccentric spot on the retina of the other eye. There is a considerable difference in the amount of light reaching the two eyes. The patient's problem is to localize the image seen with the deviated eye relative to that seen with the fixating eye.

In testing the retinal correspondence with the synoptophore, the patient is asked to superimpose images falling on the two retinas. The illumination reaching the two eyes is approximately equal (unless it is purposely reduced on one side, as must sometimes be done), and the eyes are not as completely dissociated as in the double image test. Also, the stimulus is less localized. It may, in fact, extend over a considerable portion of the retinas, and fusional stimuli may be present.

The conditions under which the double image test is performed differ widely from the conditions of natural seeing. These natural conditions are much more closely approximated in the test with the synoptophore.

This comparison of the two methods makes it apparent that one should not expect the same result with the two methods in all cases. Differences are found, their significance will be discussed later.

Tschermak's Apparatus for Determination of the Congruity Between the Motor and the Sensorial Conditions of a Squinting Patient—In order to allow the examination of the retinal correspondence under conditions existing when the eyes are used in the usual way, Tschermak-Seysenegg has devised a simple apparatus.²³ This apparatus avoids the artificial differentiation of the fields of vision of the two eyes caused by introducing colored glasses or by presenting dissimilar objects to the two eyes. It consists of a rectangular metal box with a front wall about 30 by 40 cm, which contains a lamp (fig. 6). In the center of the front wall a cross is punched out, above and below the vertical arm of the cross and in line with it are vertical slots, the upper being lined with red glass, the lower with green glass. To the right of the upper slot and to the left of the lower slot there are small blinds movable on hinges which can be so placed that the upper slot is visible only to the left eye and the lower slot visible only to the right eye. In this way a partial dissociation of the two eyes is achieved.

The patient is seated comfortably 30 cm or more in front of the instrument in such a position that his eyes are approximately on a level with the horizontal arm of the cross, and he is asked to fixate

²³ Tschermak-Seysenegg, A. *Methodik des optischen Raumsinnes und der Augenbewegungen*, in Abderhalden, E. *Handbuch der biologischen Arbeitsmethoden*, Berlin, Urban & Schwarzenberg, 1937, sect. 5, pt. 2, pp. 1427-1754 (see especially page 1557 ff).

the cross. The partitions on the slots are so placed that the slots are seen monocularly. The patient is now requested to state whether the two vertical slots and the vertical arm of the cross are lined up or whether one of the slots appears displaced, and in what direction.

If one knows the objective position of the eyes for the chosen observation distance and the retinal correspondence of the patient as determined in the after-image test, one can classify squinting patients with this instrument in the following way¹⁶

A. The patient sees the two slots and the vertical arm of the cross in one line.

(a) If the patient has no strabismus and normal retinal correspondence, there is neither a motor nor a sensorial anomaly.

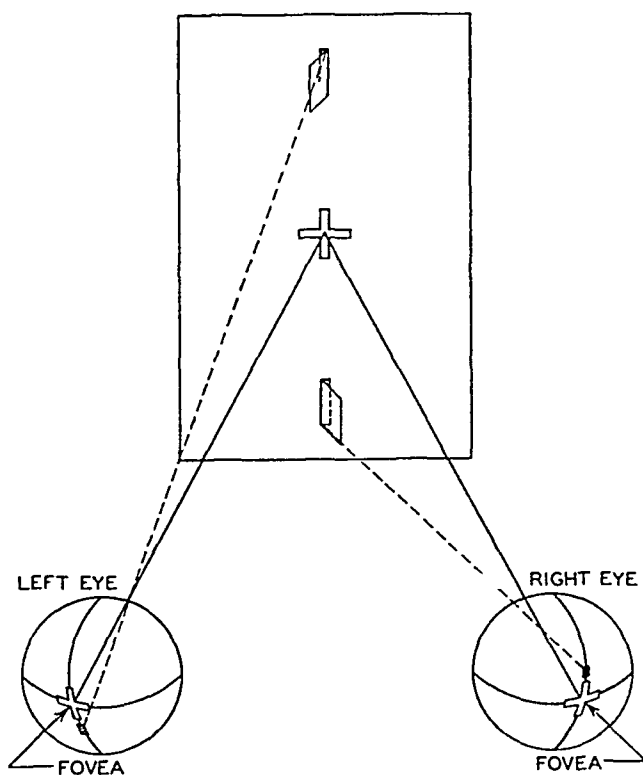


Fig. 6—Schematic drawing of Tschermak-Seysenegg's apparatus for the determination of congruence between motor condition and sensorial behavior in strabismus.

(b) If the patient has a strabismus and one eye is deviated while he fixates the center of the cross with the other eye, he has both a motor and a sensorial anomaly, but the two coincide, the patient has an anomalous correspondence adapted to the angle of squint.

B. The patient sees one of the slots displaced to the right or the left relative to the cross.

(a) If the retinal correspondence is normal, the angular distance between the center of the cross and the displaced slot is equal to the angle of squint.

(b) If the retinal correspondence is anomalous, the distance between the center of the cross and the displaced slot is not equal to the angle of squint, the angle of squint differs from the angle of anomaly, and there is no congruity between the two

I have not used this instrument in the examination of patients and have, therefore, no personal experience concerning its usefulness. It would seem to me, however, that there is no need of adding this test to the examination of squinting patients, since it does not give more information than can be obtained by the simple double image test. In both tests the fovea of the fixating eye and an eccentric element of the retina of the deviated eye are stimulated simultaneously. It must be emphasized, however, that the result of the two tests may differ in certain instances because of the more natural conditions of seeing under which Tschermak's test is performed.

Braun²⁴ was the first to employ the apparatus in examination of patients, at Tschermak-Seysenegg's suggestion. Collenza and Jablonski²⁵ used it in their studies, and Sverdllick²⁶ found the instrument valuable in examination of the retinal correspondence and advocated its use in conjunction with the after-image test²⁷.

2 DIRECT DETERMINATION OF THE VISUAL DIRECTION OF THE FOVEAS (AFTER IMAGE TEST)

Hering²⁸ saw one of the most convincing proofs for the unity of the binocular field in the following simple experiment. A small lasting after-image is produced in the left eye and the eye closed. When the right eye is now opened, the after-image will appear in the field of vision and shift with the movements of the eyes just as though the left eye were open²⁹. If the after-image was produced on the fovea, it will appear in the common visual direction of the foveas. After-images produced on the two foveas will appear in the same visual direction no matter whether the eyes are open or closed, and no matter what the relative position of the eyes is. After-images offer, therefore, an ideal oppor-

24 Braun, G. Zur Therapie und Prognose des Schielens, Arch f Ophth **120** 583, 1928

25 Collenza, D., and Jablonski, W. Sulla relazione normale ed anormale delle retine negli strabici, Boll d'ocul **16** 212, 1937

26 Sverdllick, J. Presentacion de una lampara para postimagenes y de un aparato congruente tipo Tschermak, Arch de ofal de Buenos Aires **13** 542, 1938

27 It is of interest to note that F. Bernard Chavasse (Worth, C. Worth's Squint or the Binocular Reflexes and the Treatment of Strabismus, London, Bailliere, Tindall & Cox, 1939) reproduced a stereogram for the determination of the state of the sensorial retinal correspondence which used the pattern employed in Tschermak-Seysenegg's apparatus.

28 Hering,⁹ 1863, book 3, p. 182

29 The important theoretic implications of this experiment cannot be discussed here.

tunity for the examination of the sensorial retinal relationship in cases of motor anomalies of the eyes

This experiment was suggested by Hering and was applied in the laboratory by Tschermak-Seysenegg³⁰ and on a large scale in examination of patients by Bielschowsky³¹

In the after-image test, the visual direction of the foveas, which is, of course, independent of the relative position of the eyes at the time of the test, is directly determined. This is achieved by a very simple technic. A lamp with a straight filament is mounted on a solid base in such a way that it may be pivoted around its middle and placed either in the horizontal or in the vertical position (fig 7). The central part of the filament is concealed by a metal ring which bears a white square with a fixation mark. The patient is seated at an appropriate distance

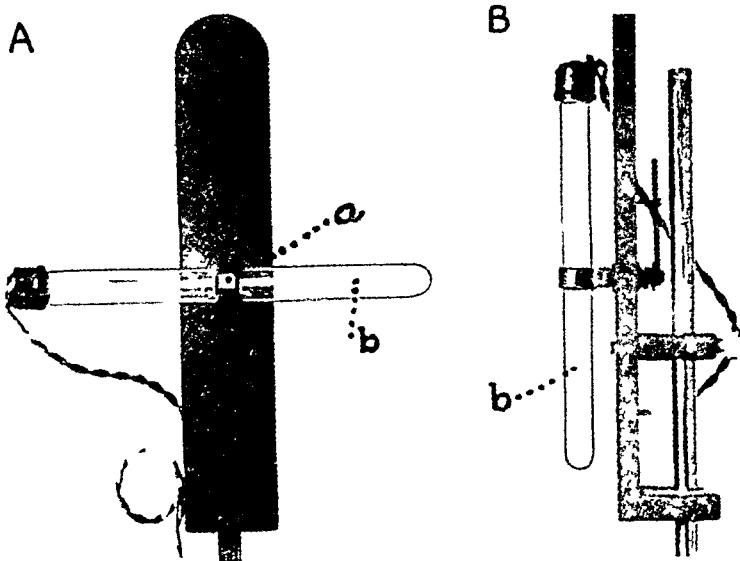


Fig 7—Lamp for the after-image test. A, front view, B, side view, a, fixation mark, b, filament

from the lamp, which is so adjusted that the fixation mark is on a level with the patient's eyes. The patient is asked to fixate steadily the mark on the lamp, first with one eye, while the filament is in the horizontal position, and then with the other eye, while the filament is in the vertical position. The time of exposure should be roughly ten seconds for each eye, and the filament must not be lighted until the patient is properly positioned. The eye which does not fixate should be well covered by the palm of the patient's hand, so that no light enters the eye.

30 Tschermak-Seysenegg, A. Ueber anomale Scherichtungsgemeinschaft der Netzhäute bei einem Schielenden, *Arch f Ophth* **47** 508, 1899

31 Bielschowsky, A. (a) Untersuchungen über das Sehen der Schielenden, *Arch f Ophth* **50** 406, 1900, (b) Application of the After-Image Test in the Investigation of Squint, *Arch Ophth* **17** 408 (March) 1937

During the exposure, a strong light stimulus reaches the principal horizontal meridian of one eye, for instance the left eye, and then the principal vertical meridian of the other eye. In neither eye is the fovea stimulated. The two successively produced after-images are now seen simultaneously, as positive after-images (bright lines) in a darkened room and as negative after-images (dark lines) in a lighted room. The region of the fovea will appear as a gap in the lines, and the two gaps will be seen in the same place if the two foveas have a common visual direction, no matter what the relative position of the eyes and regardless of whether the position of the eyes changes during the observation of the after-images. Consequently, the horizontal and vertical after-images are seen in the form of a cross with a gap in the

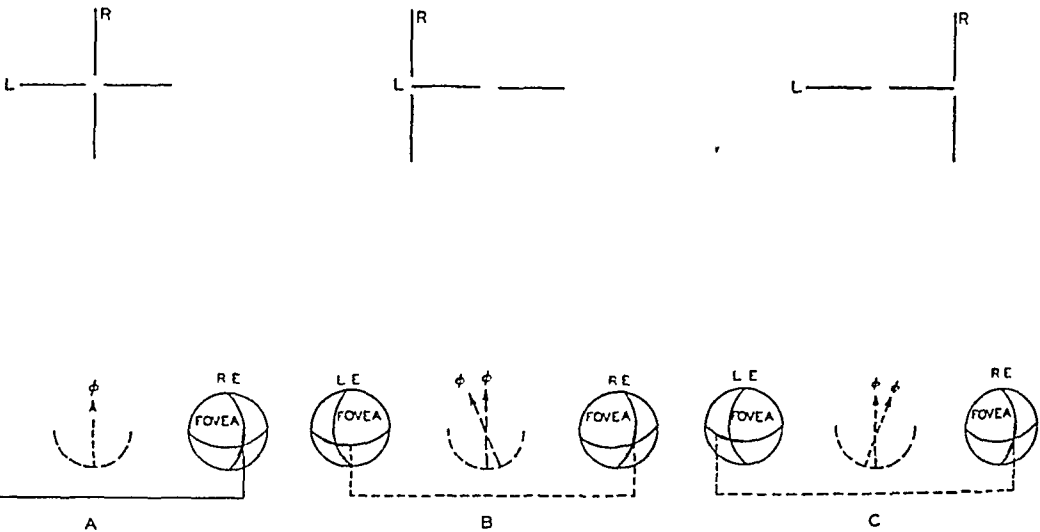


Fig 8—Result of the after-image test (A) in normal correspondence, (B) in convergent strabismus (angle of anomaly 12 degrees), (C) in divergent strabismus (angle of anomaly 12 degrees)

center (fig 8 A). If the vertical line with its gap appears shifted to the right or left relative to the gap in the horizontal line, the two foveas obviously have different visual directions, and the retinal correspondence is anomalous. Again, this relation is not influenced by the relative position of the eyes, it is, for instance, frequently the same prior to and after a successful operation for strabismus, i. e., in persons whose visual lines have been made parallel for distance.

The angle of anomaly is directly determined with satisfactory accuracy by means of the after-image test. If the length of the glowing filament is known and the patient is at a known distance from the filament, the angular size of the filament relative to the eye can be computed. With the instrument which I use, for instance, the size of one arm of the cross is 12 degrees when the distance from the patient's eye to the

fixation mark is 50 cm during the exposure. The angular size of the after-images being known, the distance between the gaps in the horizontal and the vertical line gives directly the angle of anomaly.

Figure 8*B* explains the results of the after-image test in a case of convergent strabismus of 12 degrees with anomalous correspondence adapted to the angle of squint, 8*C* shows the result of the after-image test in a case of divergent strabismus of 12 degrees with anomalous correspondence adapted to the angle of squint.

The after-image test can be performed with normally developed children as young as 4 or 5 years of age³². It is not necessary prior to the test to explain to the patient what is expected of him, but he must be instructed to fixate strictly the mark on the light bulb. He should be told that a light will flash on and that fixation must be maintained while the examiner counts from 1 to 10 during the exposure.

The examiner must observe the patient's eye during the exposure to check on the steadiness of fixation, if the patient moves his eye too much, the test must be repeated. Even patients with relatively high amblyopia (20/200 or more) can as a rule fixate sufficiently well, but patients with eccentric fixation must, of course, be excluded. The room should be lighted during the exposure so that the patient can see the fixation mark clearly, the general illumination does not interfere with the production of the after-images.

Suppression of the poorer eye or alternating unocular vision may at times interfere considerably with the after-image test. In order to minimize as far as possible the difficulties arising from unilateral suppression, I have adopted the following routine.

The better eye is always first exposed to the filament in a horizontal position. The weaker or habitually deviated eye is then exposed to the vertical filament. If the vertical after-image is always produced in the habitually deviated eye, the record of the after-images shows at a glance the condition of the retinal correspondence, the data are uniform and errors are avoided. In cases of high amblyopia of one eye, I expose the better eye for a somewhat shorter period than ten seconds and the amblyopic eye for a somewhat longer period. This causes a stronger after-image in the amblyopic eye, and the patient is more likely to be conscious of it.

After the exposure the room is completely darkened. Some patients see at once the two after-images, but the majority see either one or the other or neither. It is then helpful to flash on a light a number of times. This is almost invariably successful in making the patient conscious of

³² Sverdluck²⁶ found that the after-image test could not be performed in children under 7 years of age.

the after-images³³ He is then asked whether he sees the two lines with the gaps in the middle simultaneously and is requested to pay attention to the relative position of the gaps I usually tell the patient that I want him to draw a picture of the lines When the patient's report is satisfactory, the light is switched on, and I draw the horizontal line with its gap (using a red pencil for the positive after-images) The patient is asked to draw in the vertical line with its gap according to where he saw it He is then placed a few feet away from a large, white, well illuminated cardboard and asked to observe the negative after-images It is again helpful to flash a light on and off if the patient has difficulties in seeing them The procedure of recording is then repeated (using a black pencil) It is of interest to investigate both the positive and the negative after-images Sometimes the patient localizes one set of after-images according to normal correspondence and the other set according to anomalous correspondence The meaning of this difference in behavior will be discussed later

One sometimes encounters great difficulty in eliciting the after-image of the habitually deviated eye even if there is not a great deal of amblyopia Certain patients have such a strong mental suppression that they even suppress the after-image completely, a phenomenon which is in itself interesting and theoretically significant It is frequently helpful to ask such a patient to cover the leading eye Other patients with strictly unocular vision can alternate at will and not only can assume fixation with either eye but can elicit at will one or the other after-image by shifting the attention and changing fixation All this, of course, must not be understood to mean that the position of the eyes has anything to do with the production or position of the after-images It simply means that it is sometimes difficult for the patient to concentrate his attention on the after-image of the suppressed eye or to become conscious of it

With the vast majority of patients it is possible to obtain a satisfactory after-image test if one exerts enough patience There are, however, cases of complete alternation in which even a most painstakingly performed test does not yield the desired result of simultaneous perception of the after-images These cases are extremely interesting, but rare, and I wish to report 2 which belong in this category

CASE 1—R E M, a merchant aged 34, complained of a great deal of eye-strain and of frontal headaches There was no family history of ocular trouble, and the patient had never been seriously ill He had worn glasses for the past

33 L C Drews (Further Observations on Autofunduscopy, *Am J Ophth* 26:1143 [Nov] 1943) has recently suggested the use of his method of autofunduscopy to enhance the appearance of the after-images He also recommended exposing the filament more than once to each eye to avoid a possible occurrence of phasing, which might be detrimental to simultaneous perception of the after-images

eighteen years but had not been aware that his eyes turned out until he was about 10 years of age

Refraction and Visual Acuity—Right eye $+0.25$ D sph $\subset +0.50$ D cyl, axis 30 = 20/20 + 2, left eye $+1.25$ D sph, axis 160 = 20/20 + 2

Retinal Correspondence—In the cover test there was an alternating divergent strabismus for distance which was compensated for with prisms of 30 to 35 Δ , he was able to fixate with either eye but preferred the right eye. He could overcome the divergent strabismus by a convergence impulse, but the near point of convergence was at 15 to 17 cm and convergence was held poorly. It was impossible to elicit diplopia in the double image test, in spite of numerous attempts, in the after-image test there was complete alternation, the patient saw either the horizontal or the vertical after-image, depending on the eye which he used for fixation, and was unable to perceive the two after-images simultaneously. With the stereoscope there was alternating uniocular vision. With the synoptoscope the objectively measured angle of divergence was 25 Δ , there was no binocular perception at any angle

CASE 2—H. P. H., a white laborer aged 25, had no family history of ocular trouble except that his mother was cross eyed. His left eye had been turning in since infancy. As a baby the patient had convulsions. He wore glasses for close work in high school but had had no glasses since that time.

Refraction and Visual Acuity—Right eye $+1.00$ D sph $\subset +0.50$ D cyl, axis 180 = 20/20, left eye, $+1.00$ D sph $\subset +0.50$ D cyl, axis 180 = 20/20

Retinal Correspondence—In the cover test the patient showed a convergent strabismus of 25 arc degrees, the left eye deviated spontaneously, but the patient was able to fixate with that eye when the right eye was covered. It was difficult to elicit diplopia in the double image test, there was an indication of uncrossed diplopia of 25 arc degrees, but the patient was uncertain about it. In the after-image test there was complete alternation. When the patient fixated with the left eye, he saw the vertical after-image, when he fixated with the right eye, he saw the horizontal after-image. He never saw the two after-images simultaneously.

Another complication of the after-image test is even rarer. Certain patients with facultative divergent strabismus who have binocular fixation when the divergence is overcome by a convergence impulse see the after-images in the form of a cross (normal correspondence) when they fixate binocularly. But when their eyes are dissociated, they see the vertical after-image displaced to the right or left (anomalous correspondence). A case of this type will be given later (case 15). An uncritical observer might deduce from this finding that the position of the after-images had changed because of a change in the relative position of the eyes. This conclusion would be quite erroneous. The position of the after-images changed because of a change in the sensorial retinal relationship produced by the dissociation of the eyes. (The meaning of this interesting and important phenomenon will be considered in connection with the discussion of the essence and meaning of anomalous correspondence.)

It must be emphasized that a single after-image test has no significance beyond giving information about the condition of the retinal corre-

spondence of the patient at the moment the test is made. In order to obtain a complete picture of the condition of the sensorial retinal relationship of a patient, the test should be repeated at various times.

I have dealt here in detail with the after-image test because of its importance for the understanding of the sensorial retinal relationship in squint and because, in spite of all that has been written, it is still not generally understood. As an example, I wish to quote the description of the after-image test as given by Travers³⁴. He stated

Tschermak has described an apparatus called a *Kongruenzapparat* by which retinal correspondence can be investigated. The principle of the apparatus consists of the creation of an "after-image" in one eye which can be combined with another image in the other eye. Thus, if a vertical illuminated streak is presented to one macula and a horizontal streak to the other, the after image, in orthophoria, will appear as a cross +. If there is a squint with an abnormal retinal correspondence of the harmonious type, the after image will still be a cross, while if there is an unharmonious abnormal correspondence the after image will appear as two separate lines |—, the angular displacement between the two lines not corresponding in degree to the angle of squint. If the angular displacement is equal to the angle of squint, then there is normal correspondence.

This description is a sequence of errors. The least important of them is that Tschermak's *Kongruenzapparat* test and the after-image test are two different things. The description of the phenomenology of the after-image test is completely wrong. As the reader of this paper knows by now, the after-images in anomalous correspondence of the harmonious type do not form a cross but are separated by an angular distance equal to that of the angle of squint, but if there is normal correspondence the after-images form a cross.

It is not sufficient to point out such errors, one must attempt to discover how an author who has given so much thought to the subject came to commit them. What may have misled Travers is the fact that patients with harmonious anomalous correspondence superimpose the synoptophore targets when the arms of the instrument are at zero, while patients with normal correspondence superimpose the synoptophore targets at their objective angle of squint. But in the former case the targets are imaged on the fovea of one eye and an eccentric region of the other eye, while in the latter case both images fall on the fovea. In the after-image test, on the contrary, the gap corresponds always to the two foveas. Travers' misunderstanding is, however, deeper than that, as will be seen from the analysis of his definition of anomalous correspondence. He stated

an abnormal retinal correspondence is in all probability the result of a compromise between innate retinal local signature and the judgment of visual

³⁴ Travers, T. & B. The Comparison Between the Results Obtained by Various Methods Employed for the Treatment of Concomitant Strabismus, London, George Pulman & Sons, Ltd., 1936.

directions, and if this be so it would explain the great differences between measurements made by different methods. It is essentially a faulty judgment of visual direction.

The meaning of this definition is not clear in itself. In order to grasp what Travers had in mind, one must consult his description of anomalous correspondence. In discussing the harmonious type, he stated that the fovea, *A*, of one eye corresponds to an eccentric point, *D*, in the other eye and that

this type of correspondence would appear to indicate a harmonious working of the two eyes—in that the impulses from *D*, which resulted from incident light having the same visual direction as that falling on *A*, could presumably reinforce the impulses from *A* and so give an inferior type of binocular vision.

In unharmonious retinal correspondence, in which the angle of anomaly and the angle of squint are unequal, the fovea, *A*, and a peripheral point, *C*, closer to the fovea than *D*, will correspond.

It is clear that in this case there could be no form of reinforcement of the impulses from *A* by those from the corresponding point *C*, as the latter originate from light having a different visual direction.

It is apparent from this description that Travers thought that the lines of direction (not, as he erroneously called them, the visual directions of light) play a predominant part in relative localization, a "judgment" is made about the "visual direction," which is faulty in anomalous correspondence. At best, a compromise is reached between the "innate retinal local signature" (which apparently means the normal correspondence) and "the judgment of visual direction." This is a statement of the projection theory in crude form. A meaning is given to the lines of direction which they do not have, and the visual lines, which alone have a subjective localizing significance, are not mentioned.

The importance ascribed erroneously to the lines of direction led to the misunderstanding on the part of Travers of the after-image test. In convergent strabismus of the left eye the position of the line of direction of the left fovea is such that it would connect this fovea with a point to the right of the point fixated by the right eye. Therefore, Travers concluded, if there is "proper" judgment of the visual direction (normal correspondence), the two after-images will appear separated by the amount of the angle of squint, if there is harmonious anomalous correspondence—a "wrong" judgment of the visual direction—the patient will see a cross, as would a normal person. Actually, the reverse is true. And the reason that the after-images do not appear in the way described by Travers is that the visual directions of the fovea, and not their lines of direction, determine the relative position of the after-images. That Travers had the relative position of the eyes (the lines of direction of

the foveas) in mind in discussing the after-image test is indicated by his stating that the after-images form a cross "in orthophoria." They form a cross in any type of heterophoria or heterotropia as long as the sensorial retinal relationship is normal.

This discussion of Travers' presentation of the after-image test goes to show that the question of a clear distinction between the objective and subjective elements in relative spatial localization (lines of direction and visual lines) is not a purely academic one but is eminently practical. It leads to gross misunderstandings if this distinction is not kept in mind.

This is apparent, also, from some of the contentions raised against the after-image test by Miss Smith, of the Wilmer Ophthalmic Institute.³⁵ None of her contentions stand up under scrutiny. Miss Smith stated:

1 The test demands too much of an unintelligent patient—unwavering fixation during the ten second intervals, accurate observation and reporting of a fluctuating subjective phenomenon.

Miss Smith had apparently never used the after-image test. Otherwise, she would have known that a normal child of grammar school age, or even preschool age, has sufficient intelligence to allow the application of the test. In fact, most subjective tests used routinely in ophthalmic examinations require at least as much attention and intelligence as the after-image test, if not more. As to the fixation, it has been pointed out before that the test is impossible if the patient has no central fixation. On the other hand, small deviations in the fixation are of minor importance. They may cause the vertical after-image to appear as a broad line, but the error introduced, even if it should amount to 1 or 2 arc degrees, would still be well within the limit of error permissible in any clinical test for strabismus. She then continued:

2 The angle of false projection³⁶ depends on the angle of squint, and this angle may vary during the test. The consequent variation in the angle of anomaly is confusing to the patient, who may or may not report the change.

This statement shows that Miss Smith has misunderstood the very essence of the after-image test. In this test the visual direction of the foveas is directly determined, and this test is, therefore, absolutely independent of the angle of squint at a given moment, in contradistinction to all other methods of testing retinal correspondence, in which the result is influenced by the relative position of the eyes. Miss Smith finally stated:

³⁵ Smith, M. I. Significance of False Projection in the Treatment of Squint, *Arch. Ophth.* **21** 990 (June) 1939.

³⁶ The different terms used in connection with anomalous retinal correspondence will be considered later.

3 The test must be given in darkness or semidarkness, so the observer has few objective checks

This is not correct. The test must not necessarily be given in darkness or semidarkness, but even when this is done there is no need for objective checks, since the relative position of the eyes does not influence the results except in extremely rare cases

3 EVALUATION OF METHODS USED IN THE CLINICAL DETERMINATION OF THE RETINAL CORRESPONDENCE

Miss Smith stated in the paper from which I just quoted³⁵ that the best method for the determination of the presence of false projection is the use of the synoptophore. I am not able to subscribe to this statement. In fact, I am not prepared to say that there is one "best method" for the determination of the sensorial retinal relationship. I can only state that each method, properly applied, informs the examiner of the patient's sensorial reaction to the standard conditions of the test at a given time.

The standard conditions of the different tests have been described. They differ, and it is not surprising that they should give different results with some subjects. This may raise the question of the validity of the various tests, indeed, one may even question altogether the value of determining the sensorial retinal relationship in patients with strabismus if the results are so variable.

Instead of detracting from their value, the differences found at times in the results obtained with the various methods add to their significance. They help in establishing the prognosis as to the probability of a patient with strabismus regaining binocular vision. But in order to understand this, one must have grasped the essence of the tests as well as that of anomalous correspondence.

The essence of anomalous correspondence will be discussed later in more detail. At this point, I wish merely to state that anomalous correspondence is an attempt of the organism to adapt the sensorial condition of the visual apparatus to the anomalous motor condition in an attempt at a restoration of the binocular cooperation. Every one is born with normal correspondence, it has to be overcome in order to establish a new retinal relationship. Not every one is equally able to make this adjustment. Also, it is a slow process, and at first the new relationship is not very deeply rooted. At this stage it will be present only under normal conditions of seeing, and tests made under such conditions will more easily elicit it. But as this new, anomalous correspondence takes deeper roots, it will push the normal relationship of the visual directions more and more into the background. Eventually it may become so firmly established that it is impossible to elicit the innate, now dormant, normal retinal relationship even in tests in which

one aims at the most direct determination of this primitive, anatomically determined relationship

Reviewing the tests discussed from this point of view, one can well understand that a patient may show anomalous correspondence when tested with the synoptophore or in the double image test but will show normal correspondence in the after-image test. The first test is closest to the natural conditions of seeing, it will be easiest for the patient, accustomed to these conditions, to free himself from the innate compulsion to localize the two foveal images in a common visual direction. This will be more difficult in the double image test,³⁷ and it may become quite impossible in the after-image test.

One can thus rate the prognostic value of the tests in the following way. An anomalous correspondence found habitually in the after-image test points to a deep-rooted anomaly in the sensorial retinal relationship, and in its presence the double image test and the synoptophore test will always show evidence of anomalous correspondence. For patients with such well established anomalous correspondence the prospect of regaining binocular vision is least certain. If the anomalous correspondence is less firmly established, the patient may show more or less habitually normal correspondence in the after-image test but anomalous correspondence in the double image and synoptophore tests. Such a patient's chances of regaining binocular vision are better, and they are best if he shows normal correspondence in the after-image and double image tests and anomalous correspondence only in the synoptophore test.

In view of this situation, one might argue that the after-image test is least valuable, because the number of patients showing normal correspondence is greater than that with the other tests. This argument may be answered by saying that it is a most important bit of information to know that in certain patients normal correspondence can be relatively easily uncovered with the after-image test in spite of the fact that other tests show anomalous correspondence. On the other hand, one could argue that the double image test and, especially, the synoptophore test show anomalous correspondence in cases in which this feature is relatively unimportant.³⁸

All these arguments are rather futile. As has been shown, there can be no "best" test for retinal correspondence in cases of strabismus. The answer to the problem lies in a thorough understanding of the different tests and their proper application and interpretation.

³⁷ One must, however, not overlook the fact, discussed before, that there may also be differences in these two tests, due to the different mode of stimulation.

³⁸ "The optimist, at all events, will agree that, with the restoration of normal function in view, it is more important, in any given case, to seek out the remnant of normal sensory correspondence than morbidly to uncover the nakedness of the abnormal." (Chavasse ²⁷)

CONGENITAL VERTICAL MOTOR PARESES

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INCREASING recognition of the fact, as Wagman¹ stated, that "vertical deviations are frequently the true underlying imbalance [in horizontal deviations], the horizontal deviation actually being a secondary phenomenon" has led to a keen interest in vertical motor anomalies in recent years

Unfortunately, the elucidation of the accurate diagnosis and differential diagnosis of vertical motor imbalance is not complete. Smith² called attention to the confusion in differentiating between paresis of the superior rectus and that of the contralateral superior oblique muscle and suggested that definite diagnostic criteria be set up for this differentiation. Bielschowsky³ stated that the most frequent and important type of a single vertical motor paralysis is palsy of the trochlear nerve, and with this view have concurred Chavasse⁴ and Davis⁵. White and Brown,⁶ however, expressed the belief that paresis of the superior rectus muscle is by far the most common vertical motor anomaly, having found this condition in 75 per cent of all the vertical imbalances, and in 24 per cent of all imbalances, in an extremely large series of motor anomalies. Further, Bielschowsky³ stated that isolated paresis of the inferior oblique is "an extremely rare occurrence," while White and Brown⁶ found it third in frequency in vertical motor imbalances. Bielschowsky³ mentioned the occurrence of paresis of the inferior rectus but gave no information on its frequency, White and Brown⁶ found this paresis second only to involvement of the superior rectus in the aforementioned series.

From the Department of Ophthalmology, Beth Israel Hospital

1 Wagman, O H. *Am J Ophth* **28** 1226-1235 (Nov) 1945

2 Smith, J W. Paresis of Right Superior Oblique and of Left Superior Rectus Muscle. *Differential Diagnosis, Arch Ophth* **33** 77 (Jan) 1945

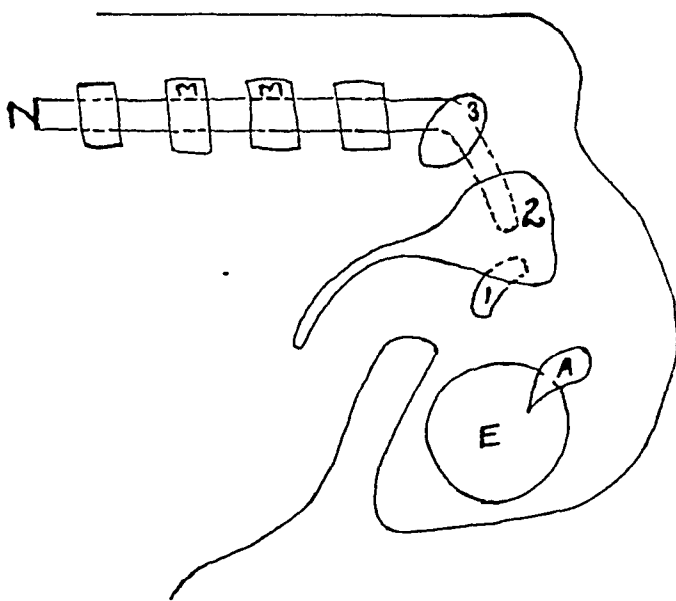
3 Bielschowsky, A. *Lectures on Motor Anomalies*, Hanover, N H, Dartmouth College Publications, 1943

4 Worth, C A. *Worth's Squint, or The Binocular Reflexes and the Treatment of Strabismus*, edited by F B Chavasse, ed 7, Philadelphia, The Blakiston Company, 1939

5 Davis, W T. Paresis of Right Superior Oblique and of Left Superior Rectus Muscle. *Differential Diagnosis, Arch Ophth* **32** 372-380 (Nov) 1944

6 White, J W, and Brown, H W. Occurrence of Vertical Anomalies Associated with Convergent and Divergent Anomalies. *Clinical Study, Arch Ophth* **21** 999-1009 (June) 1939

When such contradictions in diagnosis exist, it may be of value to investigate the etiologic factors. Paresis of the extraocular muscles may be congenital or acquired, it is with the former that this discussion is concerned. To understand the origin of congenital motor anomalies, it is necessary to review the normal embryonic development. According to Mann,⁷ the extrinsic ocular muscles are developed essentially as a condensation of the paraxial mesoderm. The earliest trace of these muscles in man can be seen in the 7 mm stage, when they are represented by a massed condensation of paraxial mesoderm surrounding the optic vesicle. However, the preceding stages are of importance in understanding the complete development. Since they are quite abbreviated in the human embryo, one must study the development of a verte-



Scheme showing head cavities of the dogfish *Squalus acanthias* (Mann, after Platt)

A, 1, 2 and 3 indicate the head cavities. 1 is the premandibular head cavity, 2, the mandibular head cavity, and 3, head cavity 3. *E* is the eye (optic vesicle), *N*, the notochord, and *M*, the somatic myotomes.

brate sufficiently simple to show the origin of the mesoderm of the head. This can be done in the embryo of the dogfish *Squalus acanthias* (figure).

In this animal, the head shows the presence of definite cavities which are evidently in series with the somites or myotomes behind them and can therefore be looked on as somitic or myotomic in value. There are four of these cavities on each side, usually numbered from before backward as *A*, 1, 2 and 3. Cavity 1 is often called the premandibular head cavity, and cavity 2, the mandibular head cavity. Only cavities

⁷ Mann, I. Development of the Human Eye, London, Cambridge University Press, 1928.

1, 2 and 3 are involved in the development of the extraocular muscles. From the walls of cavity 1, the premandibular cavity, come four main outgrowths, corresponding to the rudiments of the superior, inferior and medial rectus and the inferior oblique, that is, the muscles supplied by the oculomotor nerve. From the walls of cavity 2, the mandibular cavity, comes the rudiment of the superior oblique only, supplied by the trochlear nerve. Cavity 3 gives rise to the external rectus muscle, supplied by the abducens nerve. A consideration of this arrangement helps one to understand the underlying meaning of the human extrinsic ocular muscles, although it must be remembered that in man head cavities are not known to be present.

In other words, if one may accept the evidence of comparative embryology that "ontogeny repeats phylogeny," the undifferentiated paraxial mesoderm found at the 7 mm stage in the human embryo already represents a development of the muscle anlagen supplied by the oculomotor, trochlear and abducens nerves from the primitive first, second and third head cavities, respectively. This undifferentiated mesoderm, or premuscle mass, according to Lewis,⁸ is connected with the third cranial nerve only. The fourth and sixth cranial nerves enter at the 9 mm stage, at which time the muscle mass begins to show signs of cleavage. The differentiation gradually spreads from before backward, until at the 14 mm stage the individual muscle bellies can be distinguished as four rectus and two oblique muscles and have nearly the same position relative to the eyeball as in the adult.

However, the inferior oblique does not completely separate from the inferior rectus until later, at the 20 mm stage, according to Duke-Elder.⁹ Much later, according to the same author, at the 55 mm stage,

some of the fibers on the medial aspect of the superior rectus separate off to form the levator palpebrae superioris. At the 60 mm stage, this muscle is fully developed, and lies on the inner side of the superior rectus, it then grows laterally on a slightly higher plane, overlapping the inner edge of the rectus (75 mm), and finally (fourth month) lies above.

In this system of cleavage from the premuscle mass, it seems that the medial rectus is the first muscle to be clearly and independently differentiated. Its differentiation is soon followed by that of the lateral rectus and the superior oblique, and only these three muscles develop independently, with no subsequent offshoots. The inferior rectus is the first to be involved in subdifferentiation, giving rise to the inferior

⁸ Lewis, in Keibel, F., and Mall, F. P. *Manual of Human Embryology*, Philadelphia, J. B. Lippincott Company, 1918, cited by Whitnall, S. E. *Anatomy of the Human Orbit*, London, Hodder & Stoughton, Ltd., 1921.

⁹ Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1938.

oblique at the 20 mm stage. From the superior rectus the levator palpebrae superioris differentiates very late in embryonic development.

With this scheme of development in mind, one may proceed to the pathogenesis of congenital muscle anomalies. According to Mann,¹⁰ maldevelopment may be of three kinds: (1) failure of development of the primitive head cavities, (2) errors in cleavage or incomplete separation of the individual muscles from the common mesodermal, or pre-muscle, mass, and (3) failure of development in the central nervous system (nucleus or peripheral nerve). It is obvious that factors in type 1 or 3 must give rise to a complete paralysis of the oculomotor, trochlear or abducens type and that any congenital anomaly of the individual muscles supplied by the third nerve must be the result of "errors of cleavage in the pre-muscle mass." Thus, there are two kinds of congenital failures in muscle development: (1) complete failure of any one of the third, fourth and sixth nerve complexes, due to failure of development of the primitive head cavity or of the supply from the central nervous system, and (2) maldevelopment of the individual muscles supplied by the third nerve or of the superior oblique or the lateral rectus muscle, due to incomplete separation from the common pre-muscle mass. Whitnall¹¹ particularly emphasized the role of the latter factor.

It is probable, to judge from the writer's individual experience in finding quite a number of gross abnormalities of the ocular muscles in his series of dissections, that such are by no means excessively rare. They are explained by developmental errors in cleavage from the common pre-muscular mass.

It is the commonly accepted belief that late embryonic differentiation of an extrinsic ocular muscle renders it liable to maldevelopment. Thus, Duke-Elder,⁹ in describing the late differentiation of the levator palpebrae superioris, stated that "this origin of the levator explains the fact that it is frequently defective congenitally, and may be associated with a similar failure in the superior rectus." By the same reasoning, it might be expected that maldevelopment of the inferior oblique and the inferior rectus might also result from errors in cleavage, but, since their differentiation takes place at a much earlier stage, much less frequently than that of the superior rectus and levator palpebrae superioris. Chavasse⁴ has expressed this belief.

It will be remembered that the inferior oblique separates itself off from the inferior rectus mass. Just as the common developmental origin of the levator and superior rectus is sometimes associated with a common paralysis of the two muscles, so the inferior oblique and the inferior rectus might sometimes be affected together by a congenital paralysis.

10 Mann, I. *Developmental Abnormalities of the Eye*, London, Cambridge University Press, 1937.

11 Whitnall, S. E. *Anatomy of the Human Orbit and Accessory Organs of Vision*, London, Oxford University Press, 1932.

In other words, if one follows the muscle pareses due only to errors in pre-muscle cleavage, one would expect involvement of muscles in the following order of frequency, starting with the ones most commonly affected (1) superior rectus and levator palpebrae, by far the most common, (2) inferior rectus and inferior oblique, (3) superior oblique, (4) lateral rectus, and (5) medial rectus. So far as the vertical motor anomalies are concerned, the order would be (1) superior rectus, (2) inferior rectus and inferior oblique, and (3) superior oblique.

It is most interesting that White and Brown,⁶ in their extremely large series of vertical muscle palsies previously referred to, found a strikingly similar order of frequency. Out of a total of 661 cases of vertical muscle imbalance, the superior rectus was involved in 507, or 75 per cent, the inferior rectus, in 121, or 18 per cent, the inferior oblique, in 20, or 3 per cent, and the superior oblique, in 13, or 2 per cent.

If one may accept the belief that congenital defect of the superior oblique due to errors in cleavage of the common pre-muscle mass is rare, then one must turn to the other causes of failure of the superior oblique: aplasia either of the primitive second, or mandibular, head cavity or of the nerve unit in the central nervous system (nucleus and peripheral nerve). Mann,¹⁰ however, expressed the belief that the congenital failure of the superior oblique is rare and that the cause of the developmental defect is an aplasia of the mandibular head cavity.

Thus the weight of embryologic evidence indicates that congenital paresis of the superior oblique is rare and that palsy of this muscle probably falls into that class of uncommon complete muscular paralyses due to aplasia of the primitive head cavities. If one is to believe that palsy of the trochlear nerve is a common imbalance, one must consider it an acquired condition, the result of birth trauma or of lesions affecting the nucleus of the fourth nerve, the peripheral nerve or the superior oblique muscle itself in the early years of postnatal life. It must also be demonstrated that these etiologic factors occur with sufficient frequency in the early years of life to account for the large proportion of vertical imbalances, the incidence among strabismic children being 1 to 3, according to White and Brown.⁶

SUMMARY

Congenital pareses of the extrinsic ocular muscles are due to (1) errors in cleavage of the common pre-muscle mass, (2) aplasia of the primitive head cavities and (3) aplasia of the connections in the central nervous system. Of these, pareses of type 1 are by far the most common.

Errors in cleavage are most likely to affect those muscles which are differentiated late in embryonic development. Therefore, of the

vertical muscles, the superior rectus is considerably the most commonly affected, the inferior rectus and the inferior oblique next and the superior oblique most infrequently. There is clinical evidence to support this view.

If paresis of the superior oblique is a common vertical imbalance, it must for all practical purposes be considered an acquired lesion.

145 Central Park West

PRIMARY TUBERCULOSIS OF THE CONJUNCTIVA

G M BRUCE, M D,
AND
D LOCATCHER-KHORAZO, M D
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THIS case is reported because primary tuberculosis of the conjunctiva is rarely seen in this country. Bordley¹ was unable to find a case among over 41,000 patients treated at the Baltimore Eye, Ear and Throat Charity Hospital, Burchell² could not recall having seen the disease in his twenty years at the New York Eye and Ear Infirmary, and we have found no mention of it among the records of the Institute of Ophthalmology in New York. Isolated cases have been reported by Cohen,³ Coover,⁴ McKenzie,⁵ Sitchevska and Sedam⁶ and Thompson.⁷

REPORT OF A CASE

A 9 year old boy was admitted to the Presbyterian Hospital on Sept 27, 1937, complaining that nine days previously the right upper lid had become swollen for no apparent cause. Later the swelling had extended downward toward the ear. There had been no pain or discomfort, but he had had a low grade fever, the temperature at times going as high as 101.8 F.

The previous history was irrelevant, except that eighteen months before he had experienced an apparently similar swelling, which had subsided spontaneously in about a week. There was no history of exposure to tuberculosis, tularemia or other source of infection. No tuberculin test had ever been done.

Physical Examination—The boy was fairly well developed but rather poorly nourished, he was lively and appeared well. The temperature was 100.4 F, the pulse rate 104, the respiratory rate 20 and the blood pressure 104 systolic and 60 diastolic. Except for enlarged and cryptic tonsils and the local findings, to be described later, physical examination revealed essentially a normal condition.

There were slight edema and dusky redness over the outer two thirds of the right upper lid, with some tenderness over the lacrimal gland. A slight yellowish conjunctival discharge was present. About the middle of the upper tarsal conjunctiva was a shallow, indolent ulcer, 4 by 5 mm in size, with fairly well

From the Institute of Ophthalmology of the Presbyterian Hospital in the City of New York.

1 Bordley, J. Tuberculosis of the Conjunctiva, *Ophth Rec* **11** 368, 1902.

2 Burchell, E., cited by Sitchevska and Sedam.⁶

3 Cohen, M. Tuberculosis of the Conjunctiva, *Arch Ophth* **48** 96, 1919.

4 Coover, D. Tuberculosis of the Conjunctiva, *Am J Ophth* **3** 206, 1920.

5 McKenzie, W. Tuberculosis of the Conjunctiva, *Am J Ophth* **22** 744, 1939.

6 Sitchevska, O., and Sedam, M. Primary Tuberculosis of the Conjunctiva, *Arch Ophth* **30** 196 (Aug) 1943.

7 Thompson, J. Report of a Case of Primary Tuberculosis of the Conjunctiva, *Ann Ophth* **15** 76, 1906.

defined, reddish margins and a gray and sloughing base (fig 1) The principal lesion was surrounded by several follicles of varying sizes, at least three of which had ulcerated at their apexes The eye was otherwise normal, and vision was 20/20 Extending from the outer canthus to the tragus was an area of edema, somewhat dusky and marked by a slight roughness of the skin A large swelling (fig 2) was seen just anterior to the tragus, and continuous with it, below, was a somewhat smaller elevation These were cool, moderately tender and nonfluctuant Smaller and firmer nodules extended below these in diminishing sizes along the cervical lymphatic channels There was no discharge from Stensen's duct

The left eye and its adnexa were normal, and vision was 20/20

Laboratory Examinations—The hemoglobin concentration was 100 per cent (149 Gm), the red cell count was 4,390,000 and the white cell count 5,600, with a differential count of 76 per cent polymorphonuclear leukocytes, 18 per cent lymphocytes, 4 per cent monocytes and 2 per cent eosinophils The cells and platelets were normal No parasites were seen

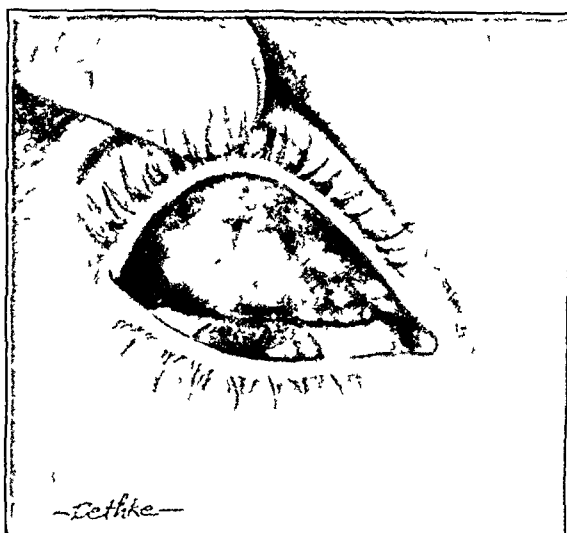


Fig 1—Primary tuberculosis of the tarsal conjunctiva in a 9 year old child

Agglutination tests were negative for *Brucella abortus*, *Eberthella typhosus*, *Salmonella paratyphoid* A and B and *Rickettsia prowazekii* The Kline reaction of the blood was negative

Tests with old tuberculin, in a dilution of 1 to 100,000, gave a positive reaction in forty-eight hours The area of erythema was 1 cm and the area of induration 0.5 cm in diameter

Roentgenograms of the parotid area showed some swelling of the soft tissues Roentgenograms of the chest, kidneys, abdomen and long bones revealed no abnormalities Roentgenologic studies were repeated frequently during the course of the illness and continued to show a normal condition throughout

Culture of material from the throat revealed a few hemolytic streptococci

Bacteriologic Investigation—Scrapings from the ulcer were examined, with the following results

Staining Method The Giemsa stain revealed no eosinophils or inclusion bodies The Gram stain showed occasional gram-positive bacilli

Ziehl-Neelsen Method A scraping was fixed with ascitic fluid and stained in the usual manner for acid-fast bacilli. Organisms similar in all respects to *Mycobacterium tuberculosis* were observed (fig 3)

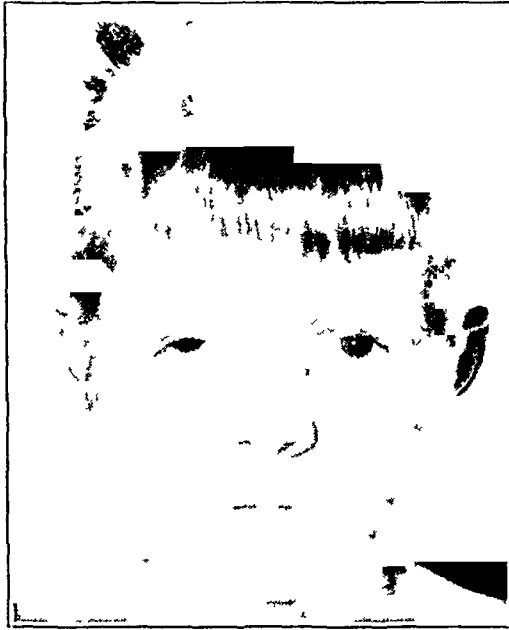


Fig 2—Preauricular swelling in a child with primary tuberculosis of the conjunctiva

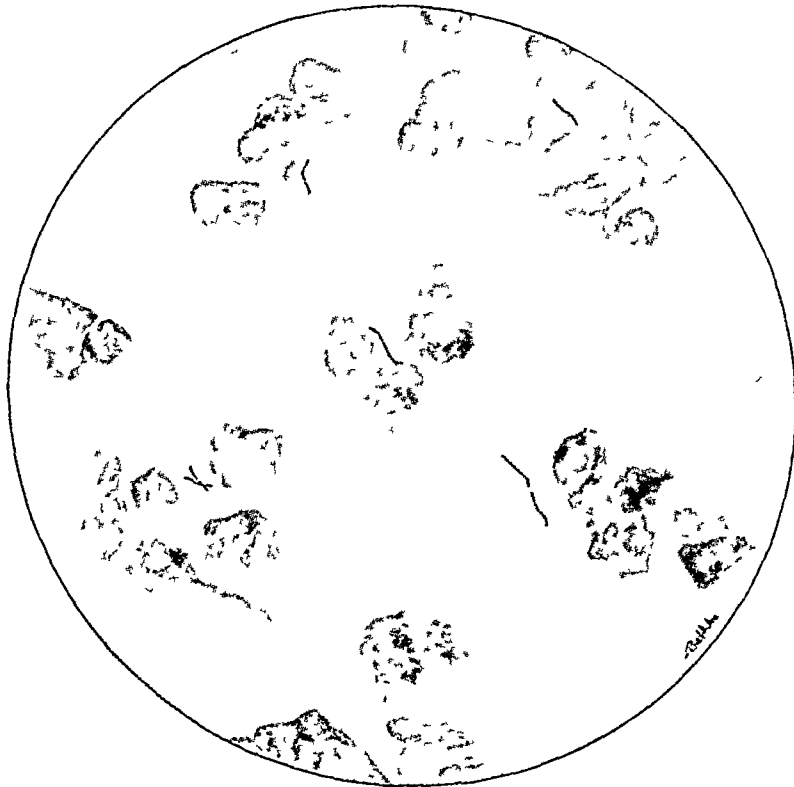


Fig 3—Tubercle bacilli in scrapings from the conjunctival ulcer (Ziehl-Neelsen method)

Cultivation Petrioff's and Frobisher's egg mediums were inoculated with scrapings. Pure cultures of *Myco tuberculosis* were obtained.

Animal Inoculation Inoculation of rabbits and guinea pigs with scrapings from the ulcer produced typical tuberculous lesions. The organisms were of the bovine type.

Treatment and Course—The eye was treated most conservatively by irrigation with a bland fluid three or four times a day. The ulcers remained stationary for about three weeks. A few additional follicles appeared nearby but did not ulcerate. Then flat granulations began to extend inward from the margins of the ulcers, the bases gradually became clean and pink, and epithelization was complete ten weeks after the lesion was first discovered. Scarring was minimal, and now, nine years after the onset of the disease, the eye is free of symptoms.

Resolution of the glandular lesions was slower. The preauricular swelling became increasingly soft, and the child had an intermittent low grade fever, the temperature never being over 100 F. About five months after the onset of symptoms, the lower and smaller of the two preauricular nodules ruptured spontaneously. The larger swelling was thereupon opened, and a small amount of creamy, greenish white pus was evacuated. No tubercle bacilli were obtained from this on culture.

Healing thereafter was slow but uneventful. No further elevations in temperature occurred, the smaller nodules disappeared, and the wounds were completely cicatrized in about four months. Four years later a tonsillectomy was performed. In one of the tonsils (which one, unfortunately, was not specified), there was observed a small area of confluent tubercles composed of epithelioid cells with little necrosis.

SUMMARY

A case of primary tuberculosis of the conjunctiva with involvement of the adjacent lymph nodes in a 9 year old child is reported. Systemic extension did not take place, and the patient recovered under conservative treatment.

Dr. Hugh Auchincloss and Dr. Howard Mason, who were in charge of the case, gave us permission to report it.

Clinical Notes

CONTRIBUTIONS TO THE TECHNIC OF CORNEAL GRAFTING

HERBERT M. KATZIN, M.D., NEW YORK

IN STUDIES which my associates and I have carried out in the Corneal Research Laboratory in conjunction with corneal transplantation, several details in the technic of the operation have been evolved which we feel are worthy of presentation

REPORT OF INVESTIGATION

Method of Cutting the Graft—The ideal method of cutting a corneal graft is one that would be completed with a sharp blade in one motion, without recourse to the use of scissors. Such a graft would always fit, without irregularities of the margin, and would involve a minimum of handling. Only a round graft could be cut in this manner, and this would best be done with a trephine.

In our experience, the Green automatic spring-driven trephine fulfills these requirements. To date, we have cut over 300 grafts from rabbit and human eyes. In over 90 per cent of these the corneal disk has been

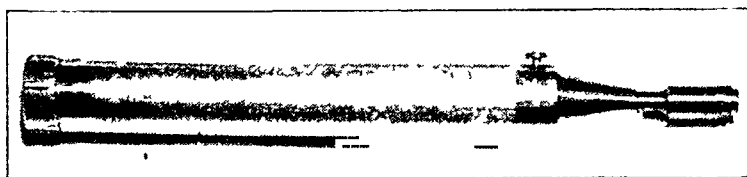


Fig. 1—Green's automatic trephine

excised completely with the trephine alone, not requiring the use of scissors. The blade is made with a protecting shoulder, so that the anterior chamber remains intact until the trephine is withdrawn. In no instance in our experience has the lens or iris been injured.

In the beginning, we filled the anterior chamber with a cushion of fibrin, before trephining, to protect the lens against injury by the blade. Later, this was discontinued as unnecessary.

The automatic trephine bevels the graft as it cuts. The action of the blade is such as to cut the upper surface on the curve of the cornea, but by the time it reaches the lower layers the pressure of the instrument flattens the cornea somewhat, so that it is more nearly flat and the area is smaller. The bevel is about 15 degrees.

It is possible to use a donor eye for two or three grafts. The first one is cut with an intact anterior chamber and so does not injure

This work was done under a grant from the Ayer Foundation.

From the Corneal Research Laboratory of the Manhattan Eye, Ear and Throat Hospital.

the underlying structures. Cutting the second will injure the lens and iris, but with care a third can also be removed. The very lightest pressure is used in operating the automatic trephine (fig 1)

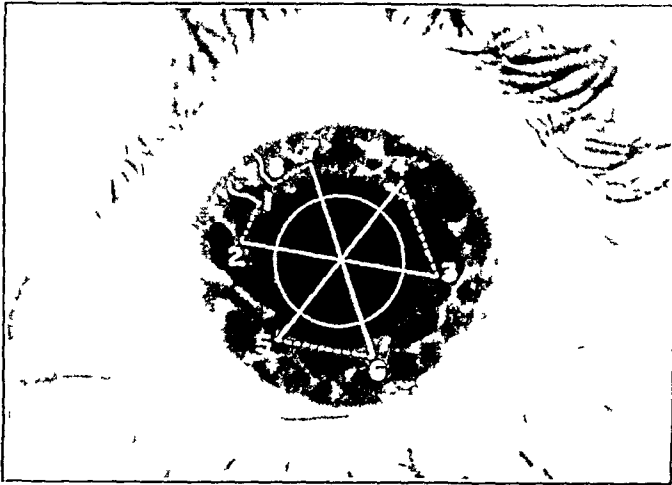


Fig 2—Diagrammatic placement of the suture

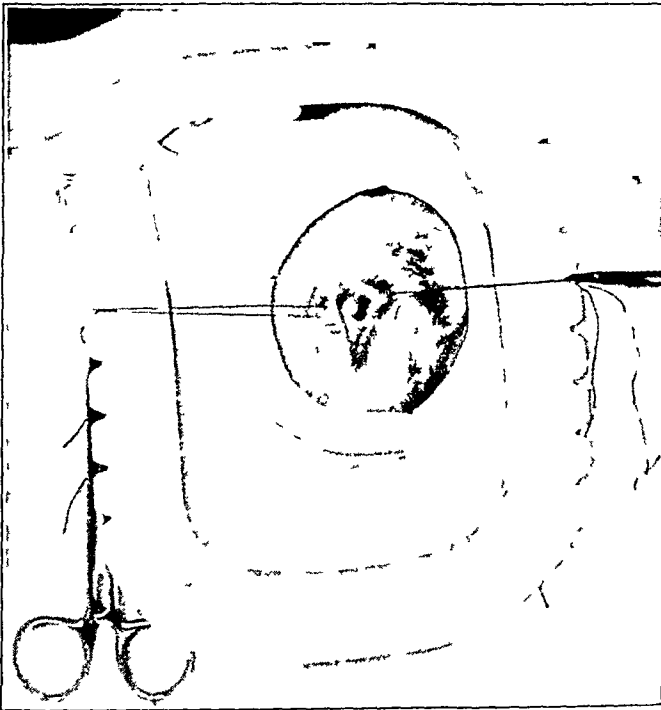


Fig 3—The suture speculum mask

Method of Fixation of the Graft—In rabbits, corneal grafting can be done without the use of fixation. The aqueous fibrin cements the graft in place until healing takes place. However, a certain percentage

of grafts are dislodged during the postoperative period and these eyes generally become infected. We have not as yet tried the fibrin method in human subjects, so we have been using a suture which gives maximum support with a minimum number of strands in a round graft. A single suture is preferred, to produce equal pressure on the graft. This suture outlines three equilateral triangles with a common apex at the center. The knot is tied at the base of one triangle, where the first suture enters and the last emerges. This suture has four points at which the needle enters the cornea, with two long bites and two short ones in the corneal substance spaced 1 mm from the margin of the graft. The short 1-2 bite is passed first, the suture is then carried directly across the center of the graft, and then the 3-4 bite is placed

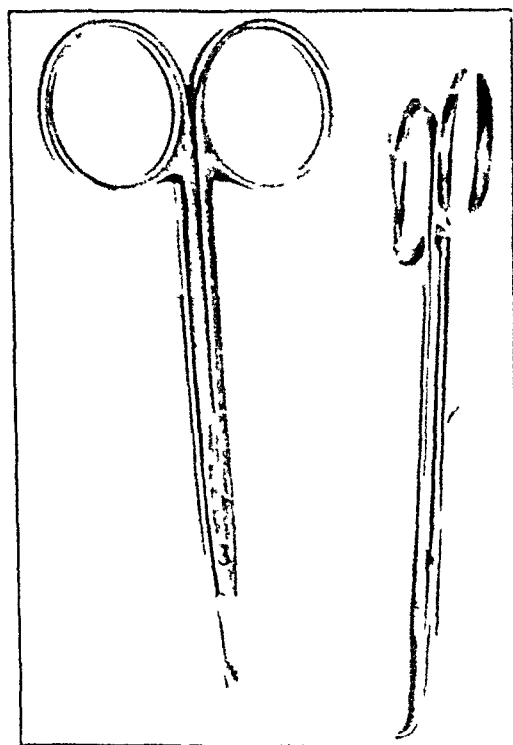


Fig. 4—Curved scissors for completion of excision of the graft

The procedure is repeated at the 5-6 and the 7-8 positions. It can be seen that the important points to have accurately placed are at 3, 5 and 7. Each of these points is an entering point for the needle, entering points are much easier to control than points of exit. Furthermore, when the suture is loosened and drawn aside so that the button can be trephined, each of the loops lies flat, the 2-3 loop, the 4-5 loop and the 6-7 loop. Each of these enters the cornea in the same direction, so that the suture material does not buckle when it is drawn aside (fig. 2).

The Suture Speculum—In order to eliminate the use of the speculum and remove the weight of the lids from the globe, sutures are passed into the lids, about 2 mm from the margin, and are fixed in the following manner. A thin aluminum mask, with a cut-out for the eyes and nose, is placed over the face on top of the drape. The outer edge of

the mask is notched to guide each lid suture, and the latter is clamped with a mosquito hemostat just below the edge of the mask (fig 3)

The Curved Scissors—When the graft is incompletely excised by the automatic trephine, so that excision must be completed with scissors, specially curved scissors are used. These are fashioned like ordinary iris scissors but with blunt tips, and the terminal 8 mm is bent on a 5 mm diameter curve, so that the blade follows the outline of the graft (fig 4)

Preservation of the Donor Eye—While experiments are under way to develop methods of preserving donor corneas for longer periods, we



Fig 5—Glass chamber

have been keeping the donor eyes in a moist chamber. This chamber consists of a glass cylinder, 40 mm in diameter by 80 mm in height. The top is fitted with a ground glass cap, and four indentations are blown in the sides, to make a constriction internally, with a diameter of 20 mm. The donor eye is kept, cornea up, resting on the constricted part. Ten cubic centimeters of sterile isotonic solution of sodium chloride is left in the bottom, so that the water vapor in the enclosed bottle keeps the cornea moist. In this manner, the donor eye can be kept in good condition in a refrigerator at 3 C for about three days. The duration depends on how freshly the eye is enucleated after death (fig 5)

Mrs Fannie Gruber and Miss Florence Schorske gave technical assistance in this work

1148 Fifth Avenue

BENCH FOR THE TEACHING OF OPHTHALMIC OPTICS

ELEK LUDVIGH, Ph D, BOSTON

THE OPTICAL bench is an essential adjunct to laboratory instruction in elementary ophthalmic optics. Nevertheless, the benches ordinarily employed are not designed for the teaching of ophthalmic optics and have many features which are undesirable for that purpose. I designed and had built an optical bench which in great measure has eliminated these undesirable features. The following discussion points out the difficulties experienced with the optical benches commonly available and briefly states how these are overcome in the bench here described.

One shortcoming of benches commonly available is that they are considerably too short. In experiments illustrating, for example, the dioptric effect of separating lenses or demonstrating the conoid of Sturm it is preferable to use lenses of relatively lower dioptric power and longer focal length than is possible with the ordinary bench, so that the adjustment of the lens and the screen is not critical. With the usual optical bench the lenses, screen and object are all crowded into a few centimeters, and it is not uncommon to see four students all trying to get their heads into the same place in space. By simply making the bench here described 2 meters long, this difficulty is avoided. (The constricted arrangement shown in figure 1 was selected to avoid excessive foreshortening in the photograph.)

A second difficulty derives from the fact that the usual optical bench provides for vertical adjustment of all its components. In the teaching of ophthalmic optics, this unnecessarily increases the likelihood that the student will misadjust the lenses. Since elementary ophthalmic optics does not consider the problem of the decentration of the crystalline lens, about the only experiment which requires that the optical center of a lens be off the optical axis of the system is one in which the prismatic effect of decentering lenses is being demonstrated. In the bench here described, the lens carriers are so designed and machined as to cause all lenses to be at the same height, and no adjustment is provided which will go out of adjustment except in the instance of one special lens carrier used to demonstrate the prismatic effect of decentering lenses.

A third difficulty, similar to the second, is attributable to the fact that the usual optical bench provides for rotation of the lens about a vertical axis. The only experiments in elementary ophthalmic optics requiring such rotation are the demonstration of astigmatism by oblique incidence and the demonstration of the prism dioptric power of

From the Howe Laboratory of Ophthalmology, Harvard Medical School, and the Massachusetts Eye and Ear Infirmary.

This study was supported in part by a grant made to the Howe Laboratory of Ophthalmology by the American Optical Company.

a prism not adjusted to provide minimum deviation. Here, again, the special lens carrier may be used for these two experiments, but the ordinary lens carrier provides for no such adjustment.

A fourth defect is introduced by the locking of the carrier on the bench. This is, of course, a practical necessity when it is anticipated that a specific optical setup will be retained for several days, or even weeks. However, a specific problem in elementary ophthalmic optics is rarely left set up for more than a few minutes, then the students

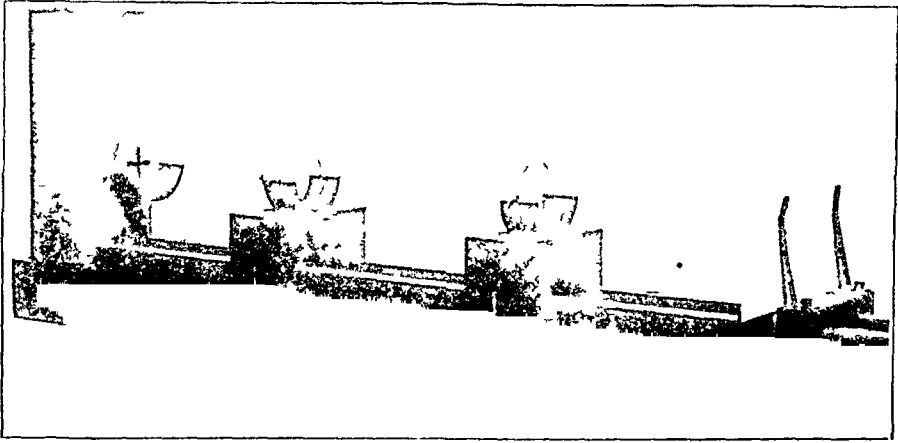


Fig 1—Bench designed for the teaching of ophthalmic optics

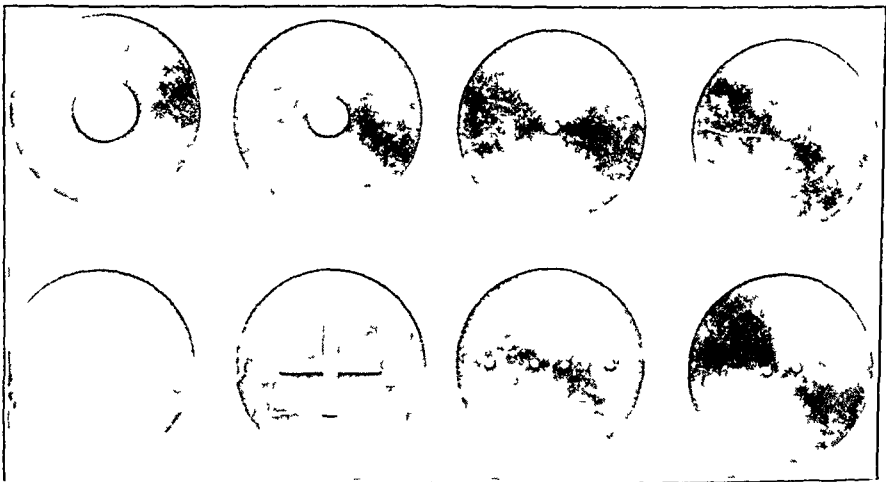


Fig 2—Apertures used with the bench shown in figure 1

proceed to the next experiment. Therefore, the locking feature is not necessary. It is not advisable because of the possibility of the lens going out of the desired position during the process of locking. This is particularly annoying when the lens carrier has a vertical member which supports the lens at a considerable height above the bench, so that a marked displacement along the optical axis of the system is produced by a slight angular change occurring during the locking process.

The bench here described has no provision for locking the carrier to the bench, and it will also be noticed in the photograph that the lens is seated low on a solid machined block, this permits smooth, easy adjustment along the optical axis without tilting of the lens. Because of this design the lens may easily be positioned to a fraction of a millimeter without distracting overshooting or undershooting of the desired position.

The fifth deficiency is that the usual optical bench does not permit lenses to be placed close enough together. In demonstrating the conoid of Sturm, the various types of astigmatic eye and the effect of placing the spectacle lens in front of the eye rather than practically on it, it is desirable that two or more lenses be placed close together. When the lens carrier is capable of carrying only one lens, the two lenses must be placed in separate carriers. These lenses cannot be placed closer together than the width of the bases of the carriers, and as this width is reduced the base becomes unstable. This difficulty is obviated in the bench here described by having several slots in each carrier, as may be seen in the photograph.

The usual optical bench is not provided with certain stops, or checks, and apertures which are useful in the teaching of ophthalmic optics. Figure 2 shows several such apertures. The upper series of apertures may be used to demonstrate the effect of reducing the size of the pupil on the effect of a given refractive error. The stop with the two holes in it can be used to demonstrate Scheiner's experiment, that with the four holes to demonstrate spherical aberration, as well as the skewness of rays in the oblique meridians of an astigmatic system. The stop with the cross-shaped aperture is, of course, employed in the study of such problems as the astigmatic eye, and the use of astigmatic dials and the cross cylinder.

SUMMARY

Because of the inherently simple requirements of optical benches intended to be used exclusively for instruction in ophthalmic optics, it has been possible to design and build an optical bench which is more satisfactory, cheaper and more rugged than the optical benches intended for general use.

This bench and the auxiliaries were made for me by Mr. C. Settino, of 7 Iowa Street, Boston.

243 Charles Street (14)

News and Notes

EDITED BY DR W L BENEDICT

UNIVERSITY NEWS

Washington University School of Medicine Refresher Course in Ophthalmology—The department of ophthalmology of Washington University School of Medicine, St Louis, has announced that its annual refresher course will be given from June 9 through June 28 of this year. The course is purely didactic, consisting of ninety-eight hours of lectures. The subjects covered will include corneal diseases, ocular therapy, surgery, anatomy and pathology, embryology of the eye, fever therapy, neuro-ophthalmology, headache, allergy, office laboratory procedures, industrial ophthalmology, the place of radiology in ophthalmology, and the association of dermatology with ophthalmology.

The tuition is \$150, and the only prerequisite is a minimum of one year's training in ophthalmology. The course is designed to refresh the busy ophthalmologist, to serve as a review for the candidate for admission to the American Board of Ophthalmology and to enable the returned physician-veteran to reacquaint himself with his specialty.

Further details may be obtained from Richard G Scobee, M D, director of graduate training in ophthalmology, Washington University School of Medicine, 640 South Kingshighway Boulevard, St Louis 10.

PERSONAL NEWS

Dr Bernard Samuels, Montgomery Lecturer—Dr Bernard Samuels, New York, will give the Montgomery Lecture at the annual meeting of the Irish Ophthalmological Society, Trinity College, University of Dublin, Dublin, Ireland, on May 22, 1947. The subject of his address is "The Problem of Sympathetic Ophthalmia."

Appointment of Dr Trygve Gundersen—Dr Trygve Gundersen has been appointed assistant professor of ophthalmology at Harvard Medical School.

GENERAL NEWS

The Delta Gamma Fraternity Project Sight Conservation and Aid to the Blind—The Delta Gamma Fraternity, an international organization of college women, announces the establishment of a fund for scholarships in the fields of prevention of blindness and sight conservation, exemplified by specialized prevention study, training of orthoptic technicians, training of teachers for sight-saving classes and training of workers for the preschool blind.

Information on basic qualifications for the various fields will be sent on request. Application blanks may be secured from Mrs Richard P Miller, 39 West Jefferson Road, Pittsford, N Y.

Advising the fraternity's council and project committee in the selection of candidates and administration of the fund is a professional committee consisting of Le Grand Hardy, M D, chairman, president of the American Orthoptic Council, Mrs Virginia S Boyce, administrative assistant, National Society for Prevention of Blindness, Miss Ruth E Lewis, professor of social work, George Warren Brown School of Social Work, Washington University, Miss Ruth B McCoy, assistant director, New York State Commission for the Blind, Lillian Ray Titcomb, M D, president of executive committee, Nursery School for Visually Handicapped, Los Angeles.

Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Blind

BLINDNESS IN TONKIN PIERRE KELLER, Arch d'opht 4: 101, 1941-1942

This paper is a review of the causes of blindness in Tonkin, French Indo-China. The causes of blindness in their order of frequency, are (1) external causes, (2) glaucoma, (3) panophthalmitis, (4) staphyloma, (5) ophthalmomalacia, (6) tumor, (7) atrophy of the optic nerve and disease of the fundus and (8) gonorrhea. Statistics indicate a great predominance of bilateral loss of vision in the cases of blindness due to gonococcic conjunctivitis, which occurred with about equal frequency in children and adults. In the cases of unilateral blindness adults predominated. Children were more frequently affected by external causes, with a greater predominance of unilateral blindness. Glaucoma affected adults only, the chronic form being responsible more often than the acute. Blindness from panophthalmitis was always unilateral and was less frequent in children than adults. Staphyloma was usually unilateral and was more frequent in adults, especially women. Ophthalmomalacia affected children only between the ages of 1 and 5 years. Tumor was as frequent in children as in adults. Neuroretinitis, most often bilateral, affected men more often, both eyes being involved. Detailed tables accompany the paper. The author points out that considerable education and organization will be necessary before much improvement can be expected. He estimates that there are about 30,000 blind persons and 30,000 one-eyed persons in the population of 7,000,000.

S B MARLOW

Conjunctiva

PENICILLIN IN GONOCOCCIC CONJUNCTIVITIS. ITS USE IN 30 CASES, COMPARED WITH THE SULFONAMIDES IN 173 CASES. P M LEWIS, Am J Ophth 29: 694 (June) 1946

Lewis concludes that the sulfonamide compounds and penicillin, especially the latter, are amazingly effective in the treatment of gonococcic infections of the eye. He recommends both in cases of severe infection.

W S REESE

VALUE OF PHLYCTENULAR CONJUNCTIVITIS IN DIAGNOSIS AND TREATMENT OF INFANTILE TUBERCULOSIS. M A DOLLFUS, Arch d'opht 4: 26, 1941-1942

The author reviews 51 cases of phlyctenular conjunctivitis, in 49 of which a positive reaction was obtained to the von Pirquet test. While local treatment of symptoms referable to the nose and throat should be carried out, the purpose of this paper is to emphasize the

necessity of not considering phlyctenular conjunctivitis a purely local condition. The author believes that in the presence of this condition a cutaneous test and roentgenogram of the chest are imperative. In 19 cases of the series studied definite contact with a source of infection was demonstrated.

S B MARLOW

SYMBLEPHARON WITH SERIOUS DISTURBANCES OF MOTILITY. REPORT OF A CASE. E V BERTOTTO, *An argent de oftal* 6:98 (July-Sept) 1945.

A patient after a fall showed a partial anterior symblepharon, with deep adhesions extending from the bone to the eyeball, thus limiting the movements of the globe, and accompanying disfiguration. The head was held in an awkward position in order to avoid diplopia and attract attention to the defect. Operations completely cured the conjunctival synechias, reconstructed the fundus of the inferior cul-de-sac entirely and largely eliminated the difficulty of directing the left eye upward and to the right.

M E ALVARO

Comparative Ophthalmology

EYE CONDITIONS AMONG CHILDREN OF PREMATURE, FULL TERM, AND HYPERMATURE BIRTH. T H EAMES, *Am J Ophth* 29:57 (Jan) 1946.

One hundred and fifty-five children who were born before completion of the normal term of pregnancy or who weighed $5\frac{1}{2}$ pounds (2,994 Gm) or less at birth are compared with 439 children born at full term or with a weight at birth of more than $5\frac{1}{2}$ pounds. These two groups are compared with a smaller group of children born during or later than the tenth calendar month. The outstanding tendencies noted are the higher frequency of low vision at all the ages studied among the children born prematurely and the poorer median visual acuity through the ninth year in the same group. The presence of somewhat comparable defects and deficiencies in the premature and hypermature groups provides a suggestion that hypermaturity may prove to be of similar, but probably less, importance than is prematurity as an initial handicap.

W S REESE

Cornea and Sclera

DIFFERENT TYPES OF METALLIC IMPREGNATION OF THE CORNEA. VERA BISCHLER, *Arch d'ophth* 4:114, 1941-1942.

The author discusses only the changes due to silver salts. They are divided into two main types: (1) changes following medication with various silver salts, either externally or internally, and (2) changes depending on the character of the work performed. The cases of silver impregnation of the cornea described in the recent literature are reviewed, together with their characteristics on examination, both without and with the slit lamp and the corneal microscope. A personal observation on a man aged 70, a silver engraver, who presented a Kayser-Fleischer ring, is described. A full bibliography is appended.

S B MARLOW

TREATMENT OF SERPIGINOUS CORNEAL ULCERS WITH ALBUCID
M. KRASNOV, *Vestnik oftal* 23:22, 1944

Krasnov treated 45 patients with serpiginous ulcer of the cornea with instillations of a 30 per cent solution of sulfacetimide every two hours or an ointment containing the drug in 30 per cent concentration. Atropine was also used. The majority of the patients entered the hospital with an advanced stage of the ulcer, more than ten days after the beginning of the disease.

There was pronounced improvement in a few days after this treatment, the hypopyon gradually disappeared, there was not a single perforation of the cornea, and the scar was usually rather fine. As a result, fairly good vision was obtained in about 40 patients. Krasnov states that weak solutions (10 per cent) of sulfacetimide were not effective enough.

O SITCHEVSKA

General Diseases

BLINDNESS FOLLOWING HAEMATEMESIS JAMES BLACK, *Brit M J*
2:920 (Dec 29) 1945

The author gives a brief review of the literature of blindness following gastrointestinal hemorrhage and reports the following case.

A coal miner aged 53 was admitted to the hospital on Aug 18, 1945, with a history that during the preceding three weeks he had felt run down, with occasional abdominal pain and the presence of a streak of blood in the stools. On August 15, while sitting at home in a chair, he suddenly collapsed and lost consciousness for ten minutes. On recovering, he vomited a quantity of bright red blood and also passed a tarry stool some time afterward. Three days later, on awakening, he found that he was totally blind in the left eye and that sight in the right eye was reduced to appreciation of hand movements. Then, in fifteen minutes the right eye became totally blind.

The ophthalmoscope revealed that the nerve heads were hyperemic and somewhat swollen (2 D), the arteries were greatly constricted, while the veins were dilated. The cerebrospinal fluid was under 200 mm of pressure. He was given 1¾ pints (710 cc) of blood of group O by intravenous drip, which was followed by gradual improvement in his general condition, but he remained completely blind.

The author emphasizes the marked contraction of the retinal arteries and expressed the belief that a routine inspection of the eyegrounds for early changes is important. An early blood transfusion may possibly arrest the changes in the eyegrounds.

ARNOLD KNAPP

Hygiene, Sociology, Education and History

BELGIAN OPHTHALMOLOGY DURING THE WAR F BONHOMME and
AGATSTON, *Am J Ophth* 29:674 (June) 1946

Bonhomme and Agatston review the history of the period of occupation, the period of liberation, the influence of the war on ocular diseases and various ocular disorders related to the war.

W S REESE

Injuries

INTRAOCCULAR FOREIGN BODIES PROBLEMS OF LOCALIZATION AND OPERATIVE PROCEDURE J KRAUS and W A BRIGGS, Brit J Ophth 29: 557 (Nov) 1945

A new localizer for intraocular foreign bodies consists of the following parts

A head rest with clamping devices attached is used to attain complete immobilization of the head. Attached to the cross bar for the forehead is a small unit designed to work in fine adjustment, carrying indicators which can be moved laterally, up and down and to and from the eye. These indicators are partly of radiopaque and partly of non-radiopaque material. X-ray cassette holders and perimeter with spot light are provided. The geometric principles of the calculations are given. The operative technic used is a modification of Stallard's necessary to suit the new localization, with an alteration in the area of diathermy application and a different scleral stitch. The problem of diathermy and magnetism is discussed, and advice is offered on how to regulate and use the diathermy apparatus to avoid complications. A newly designed forceps for extractions of nonmagnetic foreign bodies is described.

The article is illustrated

W ZENTMAYER

OPHTHALMIC TREATMENT IN THE FIELD, 1943 G C DANSEY-BROWNING, Brit J Ophth 30: 26 (Jan) 1946

An analysis was made of the 129 ophthalmic casualties treated in a mobile ophthalmic unit in the Sicilian and the South Italian campaigns. The types of wounds encountered and their treatment in the field are outlined. The results of such treatment and the final visual capacities of the treated eyes some two years later are indicated.

W ZENTMAYER

Lacrimal Apparatus

RESTORATION OF PATENCY OF THE NASOLACRIMAL DUCT BY MEANS OF A VITALLIUM TUBE W E MULDOON, Am J Ophth 28: 1340 (Dec) 1945

Muldoon reports 4 cases in which he inserted a vitallium tube into the bony lacrimonasal duct through the lower part of the sac. The procedure is designed only for cases of obstruction of the duct.

W S REESE

DACRYOSINUSITIS SIMULATING DACRYOCANALICULITIS R F PEREIRA and E E TOLOSA, Arch de oftal de Buenos Aires 20: 288 (July-Aug) 1945

The authors present a case in which a purulent discharge oozing from the upper canaliculus led to an erroneous diagnosis of dacryocanaliculitis. The patient, a woman aged 40, complained of a discharge from the right eye of long duration. Pressure on the lacrimal sac did not produce discharge of pus through the canaliculi, but when pressure

was made on the upper canaliculus pus appeared at its opening. The lacrimal passages were impervious. The patient was treated by incising the upper canaliculus. Suppuration, however, was increased after the operation. Further investigation showed that there was a direct communication from the upper canaliculus into the nasal cavity. Roentgenographic study showed the presence of maxillary and ethmoidal sinusitis.

The condition of dacryosinusitis is discussed fully. The fact is stressed that in the present case the upper canaliculus was the only one suppurating. The article is illustrated, and an extensive bibliography is given.

H. F. CARRASQUILLO

Neurology

MYASTHENIA GRAVIS AND ITS OCULAR SIGNS. A REVIEW. F. W. Walsh, *Am J Ophth* 28:13 (Jan) 1945.

This study of the ocular signs of myasthenia gravis is based on 63 proved cases of the disease, approximately 25 per cent of the patients having first consulted ophthalmologists. Walsh states that this study contributes nothing to what has already been reported regarding the ocular signs of myasthenia gravis. However, he makes the following observations. Ocular symptoms and/or signs were present in all cases. A purely "ocular" form of myasthenia gravis was observed in several instances, but in such cases there is always the possibility of spread of the weakness. The ocular symptoms and signs usually appeared early in the course of the disease, but occasionally they were a late development. Ptosis was the most constant sign, edema of the lids was an infrequent prodromal sign. Retraction of the lids was a rare complication which was observed in 1 case after chronic ptosis.

The similarity of abnormal associated movements of the lids in myasthenia gravis and those resulting from misdirection of regenerated fibers of the third nerve is noted. An explanation of the phenomena referable to the lids in cases of myasthenia gravis is not attempted. Weakness of the orbicularis oculi muscle may occur in the absence of ptosis or with it. Probably weakness in closure of the lids is overlooked more often than any other common ocular sign.

Limitation of ocular movements occurs unilaterally or bilaterally and in almost all combinations. When pupillary abnormalities are present, it is doubtful whether the case is one of myasthenia gravis. Changes in accommodation were observed in only 1 case. The visual fields and the visual acuity were not altered. The similarity of the ocular signs seen in cases of myasthenia gravis and those associated with thyroid disorders is noteworthy.

W. ZENTMAYER

Ocular Muscles

EXOPHTHALMIC OPHTHALMOPLÉGIA AND ITS RELATION TO THYROTOXICOSIS. I. MANN, *Am J Ophth* 29:654 (June) 1946.

Mann reports 18 cases in an attempt to assess the various signs and symptoms met with in so-called exophthalmic ophthalmoplegia. She concludes that the signs of excess thyroxin include loss of weight,

rapid pulse, increased basal metabolic rate, soft, moist skin, lid retraction, and lid lag (von Graefe's sign), whereas the signs of excess thyrotropic hormone of the anterior lobe of the pituitary gland consist in edema and infiltration of the orbit, lid and conjunctiva—hence, proptosis, ophthalmoplegia, fundic changes (papilledema, engorgement and macular exudate), edema of the lids, chemosis and eversion of the conjunctiva—all of which may or may not be associated with deficiency of thyroxin. The latter shows itself in a low basal metabolic rate, gain in weight, thick, coarse skin, and slow pulse

W S REESE

PARALYSIS OF THE EXTERNAL RECTUS MUSCLE TREATMENT BY
TRANSPLANTATION OF THE SUPERIOR AND INFERIOR RECTUS
MUSCLES L A GALLO and P NOVIK, *An argent de oftal*
6: 101 (July-Sept) 1945

The authors present the case history of a patient showing paralytic strabismus of the external rectus muscle of the right eye. Hummel-sheimer's operation was performed, with satisfactory results, an abduction of 60 degrees being at times obtained

M E ALVARO

Parasites

INTRAORBITAL HYDATID CYST I MARTINI Z, *Arch chilena de oftal*
1: 17 (July-Aug) 1944

A case of intraorbital hydatid cyst is reported in a woman aged 20. The condition was of five months' duration and was initiated with severe pain and redness in the right eye, accompanied with swelling at the inner angle of the fissure. The pain subsided, but the eye began to protrude and vision was lost. Later the eye was pushed entirely out of the orbit by a tumor presenting at the inner angle. The growth was removed, and the globe was replaced in the orbit. The article is illustrated

H F CARRASQUILLO

TREATMENT OF OCULAR MYIASIS WHEN LOCALIZED IN THE ORBIT
A DELMANTO, *Publicações méd* 17: 155 (Aug) 1945

In order to expel the parasite, the orifice of the entrance is enlarged a few millimeters, and a rubber tube is introduced until it meets with resistance. A solution of mercuric cyanide is injected into the external opening of the tube. The area about and the tip of the tube are coated with an ophthalmic ointment having a sulfonamide base. The tube prevents obstruction of the canal, and the air-proof ointment, together with the mercuric cyanide, produces an unbreathable atmosphere and forces the parasite to leave voluntarily in search of air

M E ALVARO

Refraction and Accommodation

LENS EFFICIENCY—A CLINICAL CONCEPT J I PASCAL, *Brit J*
Ophth 30: 291 (May) 1946

The variable of lens power not dependent on distance from the eye may be called its "efficiency" and is indicated as positive or negative

A person with corrected, as well as uncorrected, hypermetropia accommodates more, and a person with myopia accommodates less, than the emmetropic person for the same distance. On this basis, the plus lens of less power which replaces a given amount of accommodation has positive efficiency, and a plus lens of greater power which replaces a given amount of accommodation has negative efficiency.

For the subject with natural emmetropia the basic accommodation unit is 1D, but the basic accommodation unit for the subject with corrected ametropia is always either more or less than 1D. The difference is of special significance in the correction of anisometropia in the presbyopic patient. In this case the eye having the least refraction is underaccommodated and the other eye is overaccommodated for a given distance. In cases of total presbyopia the same addition for the eyes will put both in focus for a chosen distance, regardless of the refraction.

The form and thickness of the correcting lens are also factors.

A table gives the values calculated for lens and accommodation efficiency based on the results with the lens placed 20 mm from the first principal plane of the eye.

W ZENTMAYER

Retina and Optic Nerve

JUVENILE DISCIFORM DEGENERATION OF THE MACULA H LUCIC,
Am J Ophth 28:965 (Sept) 1945

Lucic reports his observations in 10 cases of juvenile disciform degeneration of the macula, including the results of microscopic examination in a case in which the condition was mistaken for a tumor. He suggests that the senile and juvenile forms are merely different degrees of the same disease.

W S REESE

ALLERGIC RETINOSIS J W BETTMAN, Am J Ophth 28:1323 (Dec) 1945

Bettman briefly summarizes the experimental evidence and clinical reports of retinal allergy and describes the case of a highly allergic patient who had edema of the macula. Vision definitely increased on two occasions within a half-hour after administration of epinephrine and finally subsided with epinephrine therapy.

W S REESE

SOLAR ECLIPSE—BURN OF MACULA E C ZORAB, Brit J Ophth 30:82 (Feb) 1946

A guardsman aged 27 observed a partial eclipse of the sun through a pair of smoked glasses. Four days later he complained of obscured vision in the left eye. Vision in the right eye was known to be poorer than that in the left, presumably due to prolonged exposure to the sun. In the left eye there was a shadow the exact shape of the uneclipsed portion of the sun. At each macula the light reflex was replaced by a dark red spot, in the center about 0.25 mm, surrounded with a pale area. Twelve days later the left macula had a central light reflex. The scotoma was still present in the right field of vision.

It is difficult to decide whether this man has a true macular burn in each eye, in the right as a result of prolonged exposure in the desert and in the left as a result of a few seconds' exposure to the sun, or whether the case is one of primary macular degeneration

W ZENTMAYER

RELATION OF CAROTID SINUS TO RETINAL CIRCULATION RISER,
PLANQUES, COUADAU and SEIGNEURIC, *Presse méd* 53:161
(March 31) 1945

Riser and his associates report observations on 50 subjects in whom they determined simultaneously the retinal arterial tension and the general arterial tension while performing various manipulations on the carotid sinus, such as digital compression of the sinus region, inhibition of the sinus by procaine hydrochloride and compression of the carotid artery below the sinus. They stress that the variation provoked in the general and in the retinal arterial tension by excitation of the carotid sinus are always synchronous and of the same amplitude. There never appeared a direct action of the sinus on the retinal circulation that could be separated from the action on the general circulation.

J A M A (W ZENTMAYER)

THROMBOSIS OF THE RETINAL VEINS AND ITS TREATMENT WITH
ROENTGEN RADIATION R CONTARDO A and A PERALTA G,
Arch chilena de oftal 1:22 (July-Aug) 1944

The authors discuss fully thrombosis of the retinal veins and describe in detail its treatment with roentgen radiation. They treated 7 patients, starting with a dose of 100 r and continuing with doses of 50 r until ten treatments had been given in 3 cases of thrombosis of the central vein and with half that dose in 4 cases in which branches of the vein were affected. In 5 of these cases the causative factor was hypertensive disease, in 1 case arteriosclerosis, and in the other, focal infection (infected tonsils). The results of treatment were gratifying, vision being improved from counting fingers to 5/5 in some cases.

The authors conclude that roentgen therapy is indicated in cases of thrombosis produced by external compression of the vessel and subsequent formation of thrombus (arteriosclerosis, neoplastic metastasis) and of occlusions due to inflammation of the walls of the vein. Treatment with anticoagulants is indicated when a blood dyscrasia is the cause or when the occlusion is brought about by stagnation produced by arterial spasm. In the last group the action of the anticoagulants must be accompanied with the use of vasodilators.

H F CARRASQUILLO

OPTIC NEURITIS OCCURRING DURING LACTATION J MALBRAN and
J B ZUBILLAGA, *Arch de oftal de Buenos Aires* 19:473 (Nov)
1944

The authors report 2 cases of optic neuritis occurring during the lactating period in 2 primiparous women, aged 23 and 24. The condition made its appearance two and fourteen weeks after labor, respectively.

Both patients suffered from severe headache. The ophthalmoscopic and campimetric findings were typical of optic neuritis. Vision was reduced to the counting of fingers. Lactation was stopped in both cases, and the condition disappeared. Normal vision was regained. The authors discuss the etiopathology of this type of neuritis.

H. F. CARRASQUILLO

HYPERTENSIVE CONDITIONS AND RETINOPATHY H. BERGLUND, Nord Med 27:1809 (Sept 14) 1945

Berglund discusses types of retinopathy which are accompanied during at least a part of the course with severe hypertension. The hypertensive disorder in which changes in the retina are especially important is essential hypertension. Ophthalmoscopy is valuable in distinguishing malignant from benign hypertension. After sympathectomy the retinopathy at times regresses almost completely. This improvement is contrasted with the equally complete, but transient, regression sometimes attained by prolonged rest in bed and administration of sedatives.

J. A. M. A. (W. ZENTMAYER)

Tumors

PRIMARY MALIGNANT TUMORS OF THE ORBITAL MUSCULATURE G. ORRRET, Arch. d'opht. 4:1 and 81, 1941-1942

The author divides these neoplasms into two types: (1) tumors with characteristics of muscle, whether or not they arise from a muscle, and (2) tumors involving one or more muscles and which are not due to extension from a neighboring growth and are not metastatic. Fibroblastic sarcoma, polymorphous sarcoma, rhabdomyosarcoma, leiomyosarcoma, round cell sarcoma and reticular sarcoma are each discussed separately, with illustrative cases from the literature. A personal case of rhabdomyosarcoma in a girl aged 9 years is presented in some detail, with photographs and complete microscopic study.

It is pointed out that these tumors can be diagnosed only by biopsy. These tumors recur rapidly and sometimes metastasize. Surgical intervention should be reduced to a minimum. The growth should be treated preferably by roentgen radiation or radium. Surgical extirpation after adequate radiotherapy may prove to be the choice of treatment.

S. B. MARLOW

PRIMARY EPITHELIOMA OF THE MEIBOMIAN GLAND WHICH INVADDED THE ORBIT, WITH DESTRUCTION OF THE EYE. REPORT OF A CASE Y. SHOJI, Arch. d'opht. 4:32, 1941-1942

The author states that in 1922 Giovanni found reports in the literature of 40 cases of tumor of the meibomian gland, 24 of which were adenomas and 16 epitheliomas. Several cases have been described in Japanese and therefore are not known abroad. Seven Japanese cases are abstracted, and a personal case is described in detail, with accompanying photographs.

S. B. MARLOW

UNRECOGNIZED INTRAOCULAR TUMORS REPORT OF TWO CASES.
C DEJEAN, Arch d'opht 4: 38, 1941-1942

The author reports the finding of an intraocular tumor in 14 eyes removed because of glaucoma, in 2 of which the presence of a tumor had not been suspected by several ophthalmologists. Unrecognized tumors of the globe appear to be rather frequent. The importance of early diagnosis is discussed. Every glaucomatous eye should be looked on as a possible site of tumor.

S B MARLOW

CONGLOMERATE TUBERCULOMA OF THE CHOROID D A SAGGESSE
and A C DECOUD, An argent de oftal 5: 84 (July-Sept) 1944

A child 2½ years of age presented a typical amaurotic "cat's eye" on the left side. The diagnosis of glioma was made, and enucleation was advised. Consent to operation, however, was not given. One month later evidences of secondary glaucoma were present. A Mantoux test in a 1:100 dilution gave a positive reaction, and physical examination revealed the presence of pulmonary tuberculosis. The mother had the same disease.

The eye was enucleated. Anatomicopathologic examination of the specimen showed a conglomerate tuberculoma of the choroid.

A discussion of this condition follows, with numerous citations from the literature. The article is illustrated with photomicrographs.

H F CARRASQUILLO

FUSIFORM MELANOSARCOMA OF THE IRIS J REMONDA and L V
FERRARIS, Arch de oftal de Buenos Aires 19: 345 (Sept) 1944

The authors present a case of melanosarcoma of the iris in a boy aged 13 who was observed for five years prior to operation. At the first examination the author observed in the iris of the right eye a lead-colored tumor, the size of a pinhead. There were other pigmented areas, which at present are not raised. The eye was otherwise normal, and the general physical examination also revealed nothing abnormal. During the first three years of observation the growth exhibited no change. After this the mass began to grow and in the six months prior to operation increased considerably in size, taking on a lobulated, cauliflower appearance. The tumor was then removed by means of a large iridectomy. Histopathologic examination of the tissue showed the characteristics of a melanosarcoma. The boy has been kept under observation, and no further change has been noted in the eye.

H F CARRASQUILLO

Uvea

ACUTE CRYPTOGENIC LYMPHOCYTIC UVEOMENINGITIS AND HARADA'S
DISEASE E BESSIERE and L CORCELLE, Arch d'opht 5: 344,
1945

Harada's disease is characterized by bilateral uveitis with detachment of the retina, general and neurologic symptoms, auditory disturbances and abnormalities of the hair and pigment of the skin. The authors point out that this syndrome is rarely complete and present 2 cases of bilateral

uveitis associated with meningeal and encephalitic symptoms but lacking auditory disturbances and abnormalities of the skin and hair. They describe a third case in which the etiologic factor was apparently similar. They believe that Harada's disease and some of these incomplete syndromes have the same origin. The etiologic factor has not been definitely demonstrated.

S B MARLOW

TRANSFUSION OF BLOOD AND BLOOD PLASMA IN TREATMENT OF TRAUMATIC IRIDOCYCLITIS B PROTOPOPOV, *Vestnik oftal* 23: 12, 1944

One hundred and twenty patients who had severe traumatic iridocyclitis were given blood transfusions every five to seven days, for a total of one to four transfusions. Most of the patients had penetrating intraocular injuries from mine fragments. In patients with intraocular foreign bodies the transfusions were given after removal of the foreign body. Protopopov believes that the blood transfusion has a stimulating effect on various tissues and organs and possibly acts as a desensibilizer. He gives the following summary:

Of 100 patients with severe traumatic iridocyclitis blood transfusion gave stable and marked improvement in 35 patients, in 44 patients the improvement was slight or transitory. In 19 patients there was no improvement, and in 2 patients the transfusion aggravated the process.

Blood transfusion as a therapeutic measure with iridocyclitis gives a better effect than the usual foreign therapy or tissue transplantation.

In some patients the transfusion was more effective than intravenous injections of methenamine, dextrose or sulfanilamide.

Blood transfusion should be combined with general and local therapeutic measures.

Transfusion of blood plasma did not improve appreciably the iridocyclitis of 20 patients.

O SITCHEVSKA

Vision

VISION IN INDUSTRY I B LUECK, *Am J Ophth* 29: 63 (Jan) 1946

Lueck uses the report of the Committee on Industrial Ophthalmology of the Section on Ophthalmology of the American Medical Association, read before the Fourth Annual Congress on Industrial Health in Jan 13, 1942, as a basis for discussion of vision in industry, especially as to individual abilities and particular industrial requirements.

W S REESE

A NEW INSTRUMENT FOR DARK ADAPTATION TESTS W KOCH, *Brit J Ophth* 29: 234 (May) 1945

Koch describes an instrument which is relatively cheap, easy to construct and apparently reasonably reliable.

After a description of the apparatus, the author calls attention to sources of error and the manner of performing the tests and gives practical hints.

The calibration of the apparatus is based on the assumption that the average final threshold of healthy children is 2.5 log units of millimicrolamberts.

After the calibration, a group of 352 normal children, aged 6 to 14 years, were tested, and these also yielded a mean final threshold of 2.5 log units of millimicrolamberts, the standard deviation being 0.161 log unit. Data on standard deviations for children are not available, but this figure corresponds reasonably well with the values for adults reported by Hunt and Hayden. These authors found among subjects less than 40 years of age a standard deviation of 0.250 log unit (mean, 2.698) and among subjects 40 years of age and older a standard deviation of 0.328 log unit (mean, 3.010). Michaelson, working with the apparatus, gives in a recent paper a mean of 3.0 log units and a standard deviation of 0.33 log unit of as normal for adults (*Brit J Ophthalm* 28: 458, 1944).

Taking the mean plus twice the standard deviation as the probable limit of normality, a final threshold of over 2.82 log units in our apparatus may be considered as suspicious, while a threshold of over 2.98 (mean plus three times the standard deviation) is definitely abnormal for children. For normal limits in adults Michaelson's paper may be consulted.

W ZENTMAYER

Therapeutics

THE VALUE OF PENICILLIN IN THE TREATMENT OF SUPERFICIAL INFECTIONS OF THE EYES AND LID MARGINS. T. CRAWFORD and E. F. KING, *Brit J Ophthalm* 28: 373 (Aug) 1944.

The purpose of this investigation was to determine the clinical and bacteriologic results of local application of penicillin in cases of conjunctivitis, corneal ulceration and blepharitis. Cases were selected to represent clinically the following four types: conjunctivitis, of some severity, with well marked injection and discharge but without secondary involvement of the cornea; conjunctivitis, again of some severity, with additional secondary corneal infiltrations, either superficial and diffuse or marginal; conjunctivitis with a single large secondary corneal ulcer or infiltration, the clinical picture being dominated by the localized corneal infection; and blepharitis, chronic and severe. All the patients were prone to frequent and disabling subacute exacerbations of the infection.

Two preparations of penicillin were used—a sterile aqueous solution containing 250 units per cubic centimeter and an ointment containing 250 units per gram of base.

As a local therapeutic measure for superficial infections of the conjunctiva, cornea and lid margins, the authors find that penicillin far excels any agent they have hitherto employed. Moreover, it would seem highly effective in cases of stubborn infection which has proved resistant to the usual methods of treatment.

From the bacteriologic viewpoint, penicillin, as employed in this investigation, eradicates sensitive organisms from the conjunctiva in a few days. It cannot, however, prevent reinfection after the cessation of treatment, and the authors saw no reason to believe that effective therapy with penicillin established any immunity to recurrent infection. In this connection, it is noteworthy that in the cases of this series in which bacteriologic relapse occurred the organisms causing the relapse were as sensitive to penicillin as were those in the original infection.

This investigation was sponsored by the consulting ophthalmologist to the army, in collaboration with the director of pathology.

W ZENTMAYER

PENICILLIN IN OPHTHALMIC THERAPEUTICS A J CAMERON, Brit M J 1:222 (Feb 17) 1945

To find out what effect the drugs usually used in clinical ophthalmology have on the activity of penicillin, the author, in conjunction with S T Cowan, made the following tests with atropine, physostigmine, epinephrine, cocaine, decicain (tetracaine hydrochloride), strong protein silver and fluorescein. These were used in twice the customary strength, except for epinephrine, which was employed in the usual strength.

The drugs under examination were mixed with penicillin (2 units per cubic centimeter) in equal volumes and were kept at 37 C for three hours. They were then pipetted into porcelain cylinders on plates sown with the Oxford staphylococcus H. The plates were incubated overnight, and the diameter of the zone of inhibition was measured. Strong protein silver was found to inhibit the growth to the same extent as the mixture of strong protein silver and penicillin. No other drug had any inhibitory action on the staphylococcus; epinephrine, however, inactivated the penicillin in the mixtures.

ARNOLD KNAPP

LOCAL PENICILLIN THERAPY IN OPHTHALMIA NEONATORUM A SORSBY, Brit M J 1:903 (June 30) 1945

In a previous article (*Brit M J* 1:114 [Jan 27] 1945), Sorsby and Hoffa gave an account of the use of penicillin for local therapy in 47 cases of ophthalmia neonatorum. As in the last 22 cases in this series so in all the 38 new cases, penicillin was used in a concentration of 2,500 units per cubic centimeter, but the frequency of the instillation was different—the substance was given at longer intervals in 13 cases and at shorter intervals in 25 cases. In 13 cases treatment was with drops of penicillin at one hour intervals for six hours, then at two hour intervals for twenty-four hours and subsequently at three hour intervals. In all these cases the response was good, but a relapse occurred in 1 case after twenty-four hours and in another after five days (in both of these cases the infection was finally cleared by a course of sulfamezathine given for five days and two days, respectively). The results do not appear to be substantially different from those obtained in the 22 cases in which the drug was given at more frequent intervals. In 25 cases drops of penicillin were instilled initially at intervals of five minutes, then every half-hour and subsequently at hourly intervals, followed by instillation at two hour intervals. This change in the frequency of application seemed desirable in order to avoid additional irrigations. It was found that when the medicine was applied at shorter intervals the tendency to the formation of pus was rapidly suppressed. Then, when the discharge had ceased, administration of the penicillin was continued at half-hour intervals until the eye was dry, then hourly for twelve hours and every two hours for twenty-four hours longer. In 2 cases of this series a distinctly poor response

was obtained. One was a case of bilateral moderately severe gonococcal ophthalmia in a premature baby. Treatment with sulfamezathine cleared the eyes within three days, only to have the condition relapse thirteen days later, and the infection was finally cleared by a second course of this sulfonamide compound. The second case was also one of moderate severity, diphtheroids were present in the smear, but the culture was negative. The condition responded well to sulfamezathine within four days.

This group of 25 cases therefore contained 2 in which no response was shown to intensive penicillin therapy and no fewer than 5 in which initial clinical cure occurred, only to be followed by a relapse, which, however, was cleared in 3 out of the 5 cases by a second course of penicillin, suggesting that too early suspension of treatment, rather than inefficacy of penicillin, was responsible for these partial failures. In contrast to these 2 cases of total failure and 5 cases of partial failure, the results in the remaining 18 cases were distinctly gratifying, the time taken for clinical cure being thirty-eight hours at the longest and twenty-five minutes at the shortest, with an average of just under ten hours. Penicillin is well tolerated by the infant eye. The author believes that general sulfonamide therapy of ophthalmia neonatorum is already obsolete as a routine procedure. The reduction of the duration of treatment from weeks, with the older methods, to days, with sulfonamide therapy, is paralleled by the reduction of treatment from several days, with the sulfonamide drugs, to as many hours, with penicillin.

The author summarizes as follows. Local therapy with penicillin in a concentration of 2,500 units per cubic centimeter proved effective in 21 out of 22 cases of ophthalmia neonatorum reported previously. In a further series of 38 cases reported here, no response occurred in 2. In 25 of the 38 cases treatment was with intensive application of penicillin (instillation every five minutes). The results were better than those obtained with the instillation of penicillin at half-hour intervals (as in the 22 cases reported previously) or at hourly intervals (as in 13 cases in the present series).

The 25 cases in which intensive treatment was employed included the 2 in which no response was obtained and the 5 in which relapse followed initial clinical cure, in 4 of these 5 cases of relapse the response to a second course of penicillin was good. Of the remaining 18 cases, clinical cure was obtained within twelve hours in 13 and within twelve to twenty-four hours in an additional 4 cases.

Severity of the clinical condition does not appear to affect the duration of treatment. Penicillin is effective against all the common organisms of ophthalmia neonatorum, including the virus presumed to cause inclusion blennorrhoea.

Local penicillin therapy is likely to replace general sulfonamide treatment as the method of choice for ophthalmia neonatorum.

ARNOLD KNAPP

Book Reviews

Why Pupils Fail in Reading. By Helen M Robinson Price \$3 Pp 257 Chicago The University of Chicago Press, 1946

In this informative book, Dr. Robinson points out that the problem of the seriously retarded reader has in the past commanded the attention and study of individual ophthalmologists, neurologists, psychologists and educators, whose approaches to the problem and subsequent interpretations have been largely limited to their special interests and experience. The resultant confusion shows the need for a coordinated study by specialists in each of these fields. Such a coordinated study forms the unique contribution of this report.

The book is divided into three major sections. The first offers a comprehensive analysis of previous studies, which reveals that assigned causes of reading disability can be grouped under the following headings: visual difficulties, intellectual and maturational status; neurologic and dominance factors, auditory, speech and language factors, physical difficulties, emotional reactions, and social and environmental conditions. The second section describes a coordinated investigation into the causal factors of reading disability in each of 30 seriously retarded readers, all of whom had a mental age of at least 7.8 years and an intelligence quotient of at least 85 on the New Stanford-Binet scale. Thus, the cases of most serious mental retardation were eliminated from the investigation, and an intellectual readiness for reading was insured. The group contributing their services to the study included a social worker, a psychiatrist, a pediatrician, a neurologist, several ophthalmologists, a speech correction specialist, an otolaryngologist, an endocrinologist, a reading specialist and the author, who acted as psychologist and reading technician. Every child was studied by each specialist, and full accounts of significant findings are given. Ophthalmologic findings are presented in detail in table IV. The psychometric reports include the mental age and the intelligence quotient on the New Stanford-Binet scale and on several nonverbal tests of intelligence as well as the reading level and the amount of reading retardation in terms of Monroe's reading index, i.e., "the ratio of the average reading grade to the average of chronological age expectancy, mental age expectancy, and the arithmetic grade. The grade expectancy is obtained by subtracting five years from the chronological age or the mental age" (page 123). Group conferences of the cooperating specialists resulted in recommendations for remedial treatment, and the attempt was made to correct one difficulty at a time, so as to evaluate the effect of each successive measure on progress in reading. The final section is a summary of significant general conclusions: findings with respect to causal factors, problems meriting further study and implications of the investigation.

No one anomaly was found to be a probable cause of the reading disability in every case, and seldom was there but one probable cause

in any case. Rather, it may be taken as a rule that the greater the number of anomalies, or hampering factors, the more serious is the retardation in reading. The probable causes most frequently assigned by the group in its final analysis are visual difficulties (50 per cent), emotional maladjustments (32 per cent) and social problems (55 per cent). Other probable causes are neurologic difficulty and endocrine disturbance (each 9 per cent) and general physical difficulty (5 per cent). Left-eyed dominance occurred in 40 per cent of the cases and mixed hand-eye dominance in 27 per cent.

The ophthalmologist will be most interested in the visual difficulties found. These included hyperopia (28 per cent), astigmatism (10 per cent) and binocular incoordination of significance (48 per cent). In the last-named group orthoptic training was helpful in promoting reading growth or in prolonging attention span for activities carried on at close range. Neither the Snellen chart nor the Keystone Visual Safety Test was found to be completely accurate in selecting the children whom the ophthalmologist identified as needing visual care. The author states (page 224) "Because of the high percentage of cases in which visual anomalies contributed to reading failure and because of the difficulties involved in identifying them, very careful attention should be given to visual examinations in the diagnosis of poor readers."

It should be pointed out that the table on ophthalmologic findings for each subject (obviously listed as reported by the ophthalmologist in charge of the case) is confused and not wholly satisfactory when examined in detail. For example, visual acuity, although determined with the Snellen chart, is not recorded in the Snellen notation, the near point of convergence is given for some subjects in inches, for others in either centimeters or millimeters, further, in a number of cases the findings on duction, phoria and near point of convergence are inconsistent.

This short review cannot hope to do justice to the wealth of interpretative and experimental material presented. It is a readable, thought-provoking report and provides an excellent survey both of the complexity of the problem and of the need for detailed diagnosis in each case to serve as a guide to remedial care and training. From the ophthalmologist's point of view, the book is the best that has appeared to date. It is so simply written that even the uninitiated reader is given a comprehensive view of the problem presented by the child who fails in reading and of what should and can be done to remedy the situation. The bibliography contains one hundred and seventy-three titles.

The reviewer is convinced that the ophthalmologist's role in many cases of reading disability is important. However, it is essential that his examination go beyond mere refractive correction. It should be sufficiently exhaustive to cover the entire functional binocular picture, particularly at the reading distance. Every effort should then be made to provide comfortable near vision, so that the child can read with a minimum of strain and fatigue for the prescribed periods of time.

GERTRUDE RAND

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DISEASE PROCESSES VERSUS DISEASE PICTURES IN INTERPRETATION OF RETINAL VASCULAR LESIONS

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BALTIMORE

I AM deeply grateful to the officers and members of the Chicago Ophthalmological Society for the honor of this lectureship and for the opportunity to pay tribute to Dr. Gifford's memory. I trust that I may be forgiven if I take a moment of the time of this scientific society to say a few personal words, for I loved Sandy very much. He was to me not merely an eminent and distinguished colleague but also a great person. I had somehow expected that he and I would grow old in ophthalmology together. Hardly a month passes but that some problem arises on which I wish I could have his judgment, some action in which I know I could have counted on his support. The subject which I have chosen is one in which he was deeply interested.¹

The past ten years has witnessed a phenomenal increase in knowledge of the pathogenesis of hypertension without a corresponding advance in the field of ophthalmoscopic interpretation. Moreover, many ophthalmologists have been compelled to devote most of their energies to war work during the past years, and the return to their more permanent interests affords an opportunity and a need for reorientation. The time seems opportune, therefore, for a general reconsideration of ideas about retinal vascular disease. What I present here contains little new information, and, indeed, no new conclusions. The old unsolved questions still remain, but if, in the light of present knowledge, they can be formulated more specifically than before, one small step toward their solution will be made.

For three generations ophthalmologists have struggled with the problem of retinal vascular disease chiefly in terms of the definition

Given as the Sanford R. Gifford Memorial Lecture, in Chicago, Feb. 18, 1946.

From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital.

1. Gifford, S. R., and Marquardt, G. Central Angiospastic Retinopathy, *Arch. Ophth.* **21**: 211 (Feb.) 1939. Gifford, S. R. Ocular Complications of Diabetes, *M. Clin. North America* **12**: 423, 1928. Gifford, S. R., and MacPherson, W. A. Classification of Vascular Fundus Diseases, *Quart. Bull., Northwestern Univ. M. School* **14**: 65, 1940. Gifford, S. R. Proliferating Retinopathy in Diabetes, *ibid.* **17**: 252, 1943. Evaluation of Ocular Angiospasm, *Tr. Am. Acad. Ophth.* **48**: 19, 1943. Eye in General Diagnosis, *Wisconsin M. J.* **43**: 509, 1944. Evaluation of Ocular Angiospasm, *Arch. Ophth.* **31**: 453 (June) 1944.

and description of ophthalmoscopic pictures They have asked themselves, What is the typical ophthalmoscopic picture of a given class of cardiovascular disease, or, alternatively, what is the typical general clinical syndrome that is associated with certain ophthalmoscopic picture? So long as the internist's and the general pathologist's knowledge of cardiovascular-renal disease was vague and diffuse, the effort to define and describe ophthalmoscopic pictures was useful and appropriate The classifications established by the ophthalmologist were not more vague or ill defined than those of the internist There were, indeed, some cases of "albuminuric retinitis" in which there was no albuminuria, some cases of diabetic retinitis in which the diabetes was mild and inconspicuous, some cases of senile changes in the fundus which had to be called "juvenile", but these exceptions were not numerous or disturbing to the *amour propre* of the profession, smugly content in the assertion that its members alone of all the medical fraternity could look at the blood vessels in the living patient and render a final verdict

With the refinement in classification and analysis by the internist, sharper disease groups have been established Ophthalmologists have attempted to keep pace with these developments and have formulated parallel classifications of ophthalmoscopic pictures I do not wish to disparage these efforts I have, in fact, contributed my own share to this work² The statistical analyses of correlations between ophthalmoscopic and general clinical findings furnish solid steps in the slow and laborious advance in knowledge of disease But it is immediately apparent to any one who attempts to apply one of the modern systems of classification of changes in the fundus that the correlations are merely statistical, that the sharper the classification is made the more individual cases which are improperly classified will be found It would seem worth while, therefore, to stop for a moment one's search for the typical and the probable and ask oneself what conclusions are to be drawn from the atypical and the concrete What are the disease processes that underlie both the typical and the atypical occurrences?

VASCULAR DISEASE PROCESSES

Up to the present, four major, potentially independent, processes of vascular disease have been recognized (1) senescence, (2) atherosclerosis, (3) the hypertensive arteriosclerotic process and (4) diabetic vascular disease I am leaving out of this account such rare phenomena as periarteritis nodosa and Monckeberg's sclerosis With respect to these four major processes, one must ask What are the

2 Friedenwald, J S (a) Retinal Arteriosclerosis, in Cowdry, E V Arteriosclerosis, New York, The Macmillan Company, 1933, (b) Retinal and Choroidal Arteriosclerosis, in Ridley, F, and Sorsby, A Modern Trends in Ophthalmology, London, Butterworth & Co, Ltd, 1940

ophthalmoscopic signs by which they are recognized, and how reliable are those signs? What is known as to the mechanism of their development? To what extent are these mechanisms dependent on or influenced by local processes? To what extent are these potentially independent mechanisms also potentially interrelated?

Changes of Senescence—The concept of the senescent changes in the retinal vascular tree³ is, in the first place, based on the ophthalmoscopic pictures seen in the fundi of aged persons. In broad outline, the typical ophthalmoscopic picture of senescence includes vessels which are narrow and straight, which branch at acute angles and which show diminished intensity of the vascular light streak. Retinal luster is decreased. There are associated degenerative changes, such as colloid excrescences on the lamina vitrea and atrophic changes in the choroid about the optic disk, in the macular region and in the periphery of the fundus. How reliable are these signs as indications of senescence of the cardiovascular system, or even of senescence in general? It is common experience to see narrow, straight arteries in middle-aged people with atherosclerosis and without other signs of exaggerated general senescence. Furthermore, the high incidence of atheroma of the central retinal artery at the point of its passage through the cribriform disk and within the optic nerve immediately behind the disk has been well established. A detailed correlation of the caliber and tortuosity of the retinal branches with postmortem studies of the structural changes in the artery within and behind the disk is still lacking, but there is at least presumptive evidence that the narrow, straight retinal arteries of the aged are to be attributed to atherosclerosis rather than to senescence.

In this connection, it should be pointed out that Wagener and his colleagues stated that the picture of narrow, straight arteries was characteristic of the first stage of essential hypertension and expressed the belief that it was due to a diffuse spastic contraction of the ophthalmoscopically visible arterial tree. My own experience has led me, on the contrary, to the conclusion that in the early stages of essential hypertension without atherosclerosis the visible portions of the retinal arterial tree are either normal or, in some cases of the severest form, dilated.

The atrophic and degenerative changes occur not only in the aged but also in presemile persons. In fact, their occurrence without senility is so striking that ophthalmologists have been forced to set up separate disease categories for these so-called juvenile cases. Histologically, these atrophic and degenerative conditions are associated with fibrosis

³ Friedenwald, J. S. *The Eye*, in Cowdry, E. V. *Problems of Ageing*, ed. 2, Baltimore, Williams & Wilkins Company, 1942.

and hyalinization of the chorioidal capillaries. The question is still unsettled whether these histologic changes are specific evidence of senescence of the affected tissues, independent of systemic disease, whether they represent a special vascular disease process, distinct from the four major categories previously enumerated, or whether they are the form that the atherosclerotic process takes when it involves vessels of capillary dimensions. The last possibility has certainly not been ruled out and is, in fact, subject to experimental approach, for a quite pure form of atherosclerosis can be produced in rabbits experimentally. In any case, the ophthalmoscopic finding of these so-called senile degenerative conditions is an unreliable index of the state of senescence of the patient's vascular system as a whole.

Finally, there is the senile loss of retinal luster. The explanation of this optical phenomenon involves the solution of a paradox. Biochemical studies have shown that the retina, like other fixed tissues, tends to lose water with advancing age. Its index of refraction should, therefore, increase, and, other things being equal, its luster should also increase. The solution of this paradox must lie in senile changes in the vitreous, rather than in the retina. A possible optical explanation need not be elaborated here, but it is at least apparent that this feature of the senile fundus picture is not concerned with the state of the connective tissue system, including the "vital rubber" of the cardiovascular system. It is, of course, probable that a statistical correlation could be established between the decline in retinal luster and the loss of elasticity in the vascular tree. The passage of the years brings about changes in all tissues, but if the tissue systems are not identically influenced the correlation between vascular elasticity and the calendar age or between vascular elasticity and the facial and bodily appearance may be closer and more reliable than that between vascular elasticity and retinal luster. The fact that retinal luster declines more rapidly in myopic than in hyperopic persons indicates that local factors exert an important influence.

There is, in fact, good evidence that the rate of senescence of different tissue systems is more or less independent. Patients with senile dementia do not, as a rule, show corresponding signs of unduly rapid senescence of organs other than the brain. Their fundi in general have an appearance that correlates much more closely with their calendar age than with their state of mental decline. Conversely, patients with advanced senile changes in the fundus do not in general show a corresponding mental deterioration. There are some organs, like the notochord and the hyaloid vascular tree, which undergo senescence in embryonic life, others, like the gonads, which have a life span considerably shorter than that of the organism, as a whole, and still others,

like the eye, which have a longer potential life span than that of the organism

In summary, the ophthalmoscopic picture of the senile fundus is made up in part of aspects which can with a high degree of probability be attributed to atherosclerosis, in part of the consequences of capillary fibrosis, which may or may not be an atherosclerotic manifestation, and, in part of senile changes in tissues which are not components of the connective tissue and vascular systems

This argument obviously begs the question as to whether atherosclerosis and capillary fibrosis are themselves direct or indirect expressions of the process of senescence. A categorical answer cannot be given to this question at the present time, but it seems unlikely that the connection is a direct one. The most general attribute of senile change is the loss of water and of elasticity in the affected tissues,

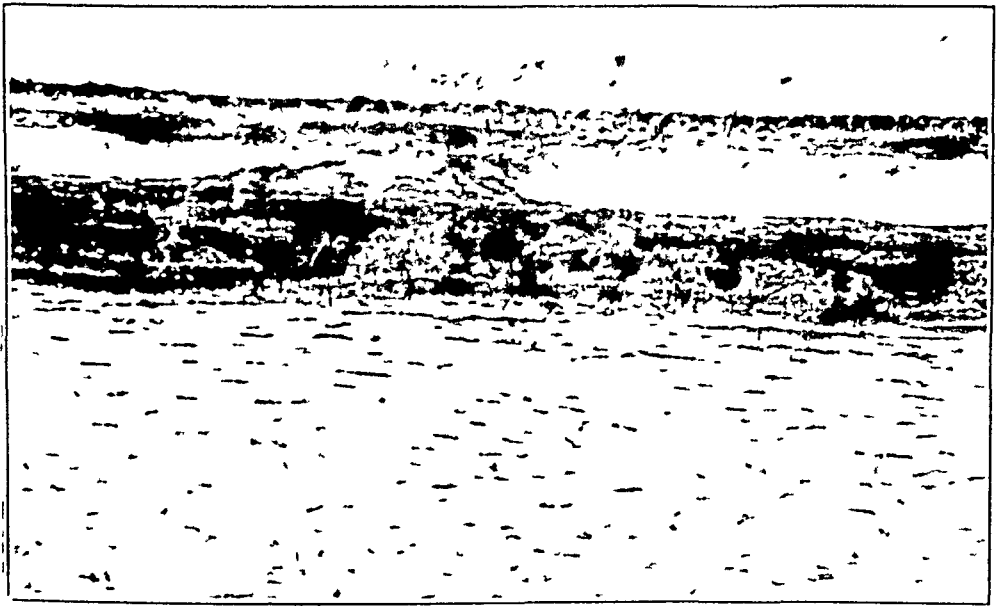


Fig 1—Lipid infiltration of the choroid in experimental atherosclerosis in a rabbit

phenomena which do not appear to be intimately connected with the atherosclerotic process. Experimental atherosclerosis in rabbits is not associated with a general loss of water and of elasticity of the body tissues. On the other hand, histologic study of aging tissues reveals an increase in fibrous trabeculae and of other relatively inert colloidal deposits which encroach on the shrinking microcosm of still vital tissues. Whether these phenomena are related to the atherosclerotic process remains an open question. A number of years ago I had the opportunity to study the ocular tissues of a series of rabbits in which Dr W A Perlzweig, of Duke University, had produced experimental atherosclerosis. A number of these specimens showed extensive lipid infiltration of the choroid. As is well known, these animals also have

a lipid arcus in the cornea. It was evident that experimental atherosclerosis entails a pathologic process more widespread than the mere formation of localized atheromatous plaques in the major vessels. But the fact that there is still a large field of potential investigation in relation to the extent and pathogenesis of the atherosclerotic process should not lead one to overestimate the reliability of ophthalmoscopic findings in the diagnosis of senescence.

Atherosclerosis—The distribution of atheromas in the vascular tree is spotty and irregular. In no two cases is the pattern identical, though certain points of predilection are fairly well established. No satisfactory explanation has been offered for these points of predilection. It is commonly stated in the textbooks that the frequent occurrence of atheromas at arterial bifurcations is related to special strains occurring at these points, but no hydrodynamic evidence has been advanced to indicate that special strains would in fact exist at these points. Actually, at the orifice of a branch the lateral pressure must be higher than average at the downstream side of the orifice and lower than average on the upstream side, but atheromas commonly surround such orifices, without regard to the slight local differences in pressure. It is likely, therefore, that any explanation of the peculiarities of atheromatous predilection must be based on local anatomic predispositions rather than on special hydrodynamic strains.

One such point of predilection is at the passage of the central retinal artery through the cribriform disk. The narrowing of the vascular lumen peripheral to such a partially obstructive lesion has already been mentioned. If in relation to the atherosclerotic process the vessel also shrinks longitudinally, the retinal branches will be not only narrow but also straight, and the angle of their bifurcations will be narrowed.

This is the ophthalmoscopic picture commonly seen in elderly arteriosclerotic persons with moderate hypertension, the degree of hypertension being closely correlated with the degree of narrowing. A number of years ago^{2a} I suggested a possible explanation of this correlation in terms of a close relation between the degree of atherosclerosis of the central retinal arteries and that of the arteries of the brain. If this is correct, the hypertension in cases of senile arteriosclerosis is compensatory and presumably neural in mechanism. No evidence has since been brought forward on this point, and the question still remains open.

The suggestion made here is in contradiction to that of Wagoner,⁴ who described senile arteriosclerosis as showing reduction of caliber of the retinal arteries and veins without arteriovenous constriction but stated that "there is no actual narrowing of the lumen, so the apparent

4 Wagoner, H. Observations on Retinal Arteriosclerosis, *M. Clin. North America* 7: 275, 1923.

reduction in calibre must be owing to decreased transparency of the walls”

The interpretation in cases of this type is further complicated by the fact that in atherosclerotic persons atheromas not infrequently develop in the major renal arteries. When such a lesion is sufficient to mimic a Goldblatt clamp, a humoral and renal phase of the hypertensive disease will be superimposed on the previous atherosclerotic phase. Thus, in these cases the transition from essential to malignant hypertension can be reproduced, and in the final state an arteriolar sclerosis may be superimposed on the preexisting atherosclerotic disease. I believe that this course of events accounts for many of the cases in which, both ophthalmoscopically and at autopsy, a mixture of these two processes is shown. An alternative explanation for this common association is given by many recent authors, who assume that hypertension, by producing more mechanical stress on the arterial tree, leads to early and widespread atherosclerosis. Against this interpretation is the fact that patients with coarctation of the aorta carry high pressures in the arteries of the head and arms for many decades without development of atherosclerotic changes.

While the point of maximal predilection for atheroma in the retinal artery is at or behind the optic disk, small lesions of a similar type are not uncommon in the vessels that can be viewed with the ophthalmoscope. Since, as a rule, the wall of the vessel remains invisible, the ophthalmoscopic evidence produced by such a lesion is a local constriction in caliber. Much restraint is required in the interpretation of this feature of the ophthalmoscopic picture, for similar local constrictions in caliber can also be produced by a localized spasm of the arterial wall and by hyaline arteriolar sclerosis. Even the persistence of such a localized constriction for days or weeks does not exclude the possibility of spasm, for previously persistent constrictions disappear promptly in some cases after splanchnic sympathectomy. On the other hand, the spontaneous disappearance of a localized constriction does not exclude the possibility that it was atheromatous, for an atheroma may become partially organized and absorbed. It is only when an opaque spot in the vessel wall is seen associated with a local constriction in caliber that one can assert with considerable confidence that the lesion is atherosclerotic, not spastic. Careful examination of these regions with red-free or monochromatic green light not infrequently reveals a slight opacity, which is less readily visible with white light. When this type of retinal vascular lesion is widely developed, white streaks of appreciable length may be seen on one or both sides of the blood column. In such a case the differential diagnosis between atheroma and hyaline degeneration may at times be difficult. The more diffuse and homogeneous the lesion, the more closely the picture characteristic of hyaline arteriolar sclerosis

is approached. The fact that the two types of lesions may be present simultaneously adds to the diagnostic difficulties.

When the atherosclerotic change affects a retinal artery at the point where it crosses a vein, endothelial proliferation may occur within the vein, and narrowing of the venous lumen may be visible not only at the point of crossing but extending upstream and downstream from that point. The relation of these endothelial proliferations to venous occlusion has been demonstrated by several authors.⁵

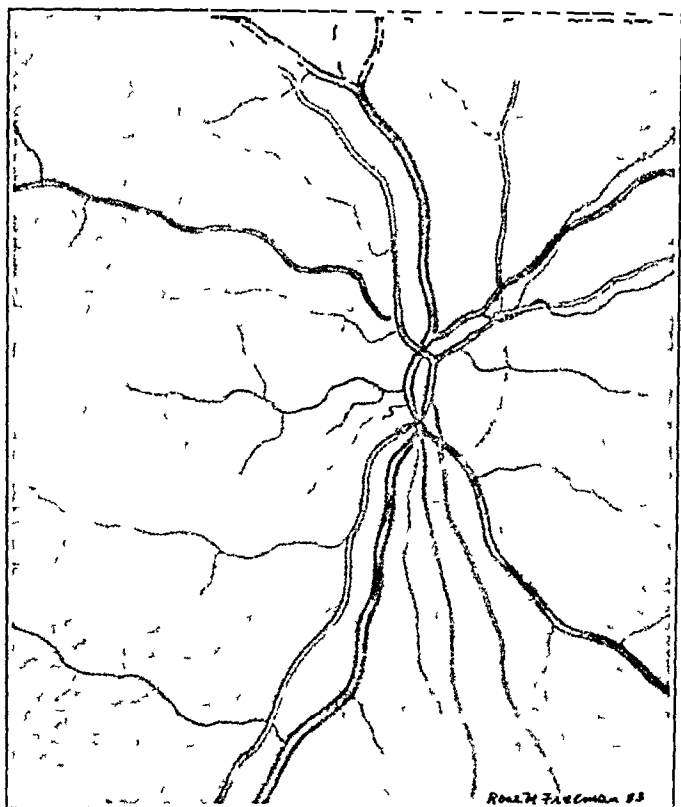


Fig 2—The fundus in a case of atherosclerosis with hypertension. The retinal arteries are narrow and straight and branch at relatively acute angles. There are localized caliber constrictions in many of the vessels (possibly due to local atheromas, but this is not certain, since increased visibility of the vessel walls was not observed).

The patient, a white man aged 77, had a blood pressure of 190 systolic and 130 diastolic. There were cardiac enlargement and auricular fibrillation but good compensation. He entered the hospital because of trigeminal neuralgia, for which operation was successfully performed. The urine showed an occasional trace of albumin and some hyaline and granular casts but could be concentrated to a specific gravity of 1.027. The patient showed obvious peripheral signs of atherosclerosis.

⁵ Verhoeff, F. H. Obstruction of the Central Retinal Vein, *Arch. Ophthalmol.* 36:1, 1907. Koyanagi, Y. The Significance of Crossing of Vessels in the Production of Thrombosis of Branches of the Central Retinal Vein, *Klin. Monatsbl. f. Augenheilkd.* 81:219, 1928.

Many cases of atherosclerosis are uncomplicated by hypertension. In such cases scattered lesions of the type just described may be seen in the fundi without the general narrowing of the retinal arterial tree. It must be borne in mind, however, that the distribution of atheromatous lesions in individual cases follows a most irregular and unpredictable pattern. Usually retinal atherosclerosis is associated with equally widespread general atherosclerosis, but in the occasional patient the presence or absence of retinal atheromas may lead to a false prognosis. The best preserved man of 87 that I know had at the age of 65 a localized atheromatous plaque in one of his retinal arteries and occlusion of a retinal venous branch. In the following twenty-two years he had had no other signs or symptoms of atherosclerosis, either local or general. Thus, even the more dramatic local vascular accidents furnish relatively

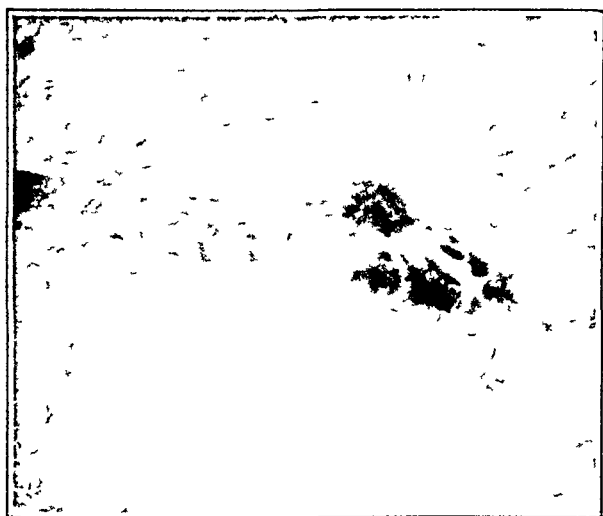


Fig 3—Flat preparation of the retina stained for fat, showing an atheroma in an arteriole. The diameter of the arteriole is approximately 60 microns. Magnification, $\times 100$.

uncertain prognostic guides. The important question is not how severe is the local lesion, but how widespread is the process. A small number of atherosclerotic persons exhibit crops of petechial hemorrhages and hard white exudates, resembling those seen in diabetic persons. This group of patients will be discussed in a later section.

Little study has been directed toward the ultimate course of the atheroma itself. It appears to be generally believed that an atheroma once formed remains indefinitely unchanged. This certainly is not necessarily true. Infants under 2 years of age commonly show atheromas in the aorta at autopsy. Infants who survive into childhood almost surely must have had similar lesions which disappeared completely. In experimental atherosclerosis practically complete recovery has also been noted. In the retinal arteries I have seen localized constrictions in

caliber with opacification of the wall of the vessel persist over a year and then disappear completely. The complete resolution of atheromas cannot, of course, be confirmed histologically, but an alternative method of healing can be well demonstrated. One frequently finds atheromas in which

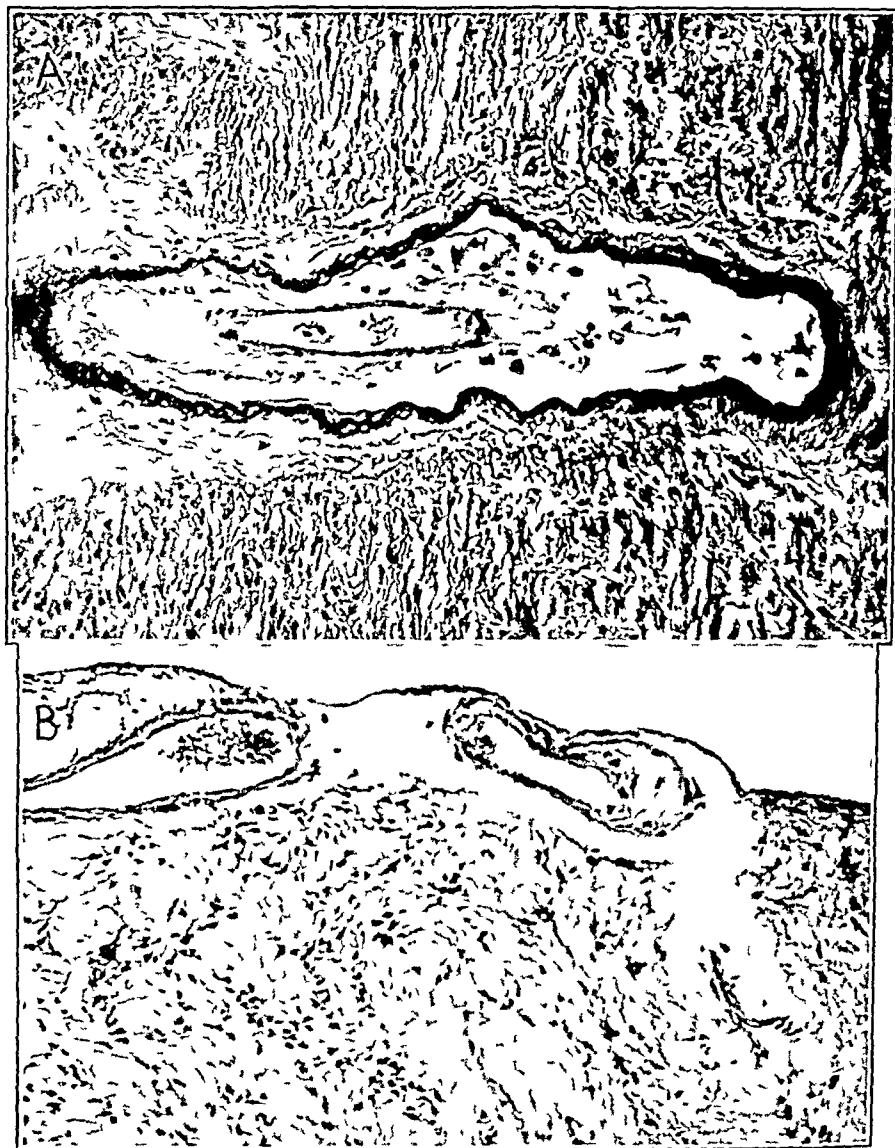


Fig 4—*A*, atheroma of the central retinal artery with beginning fibrosis, *B*, atheroma of the major retinal artery with subendothelial fibrosis

the foam cells are being replaced by a subendothelial scar, which in its crescentic form shows the flattened pattern of the original hillock.

Atherosclerosis of the choroid is a much neglected subject. It has been known for years that the choroid resembles the spleen in the frequency with which its arteries show hyaline degeneration of the

media. Changes of this type are regularly seen in the choroid beginning in the fourth or fifth decade, even in the absence of generalized arteriolar hyalinization. While this is the dominant form of choroidal

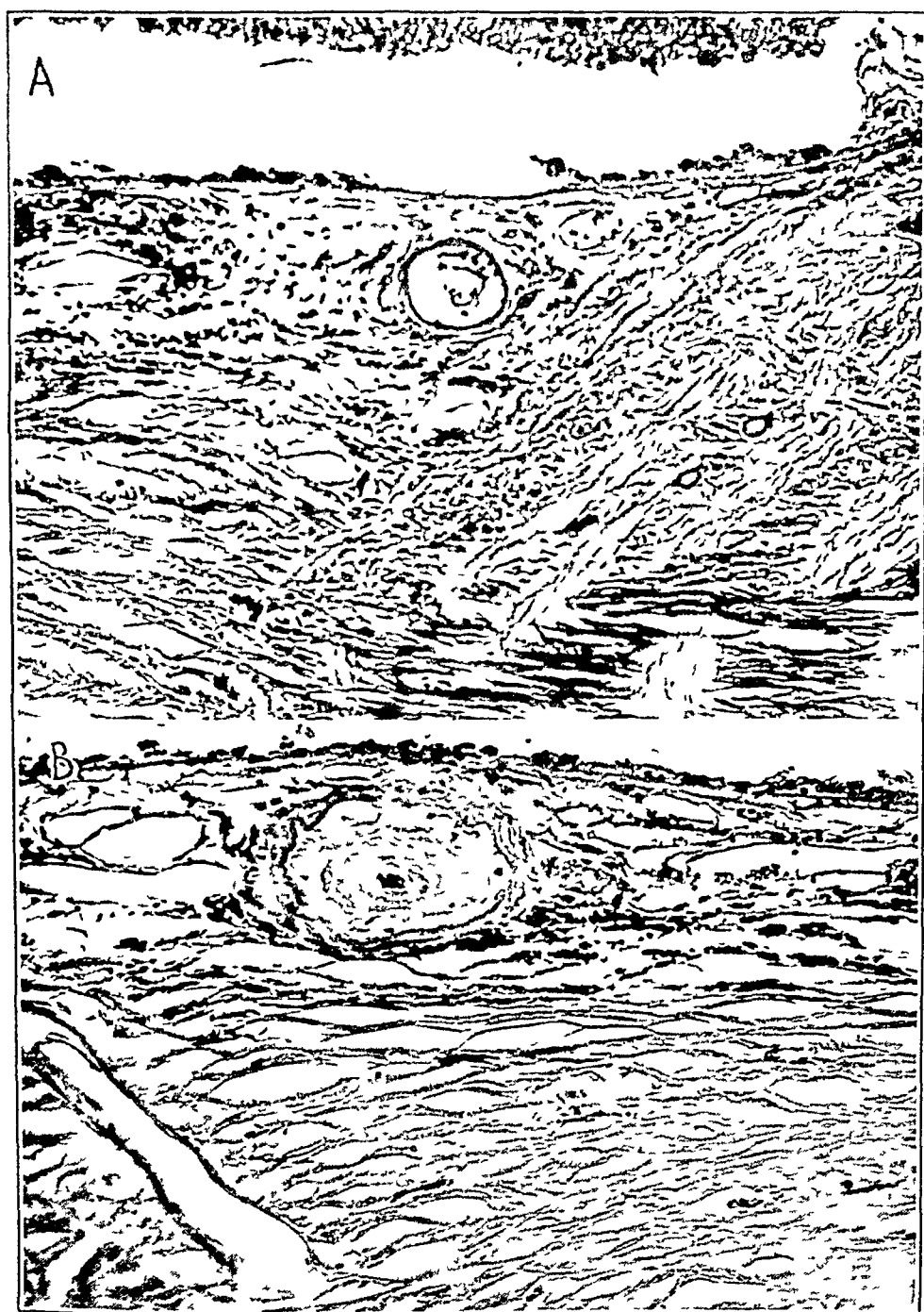


Fig 5—*A*, atheroma of a choroidal artery, *B*, atheroma of a choroidal artery with advanced fibrosis

vascular change, atheromas can also occur. The clinical ophthalmoscopic signs of choroidal atherosclerosis have not even been looked for.

In summary, ignorance of the ocular manifestations of the atherosclerotic process still largely outweighs proved knowledge. In those

cases in which lesions are exhibited in the ophthalmoscopically visible portion of the vascular tree the diagnosis can be made with a relatively high degree of certainty. The signs of sclerosis of the central vessel behind the cribiform disk are still disputed. This was, perhaps, an academic issue when the present differences of interpretation were first formulated, fifteen to twenty years ago, but it becomes an urgent practical consideration in so far as ophthalmoscopic findings are used as guide in the selection of cases for sympathectomy. The relation of atherosclerosis to subendothelial fibrosis and to capillary fibrosis and hyalinization remains unclear.

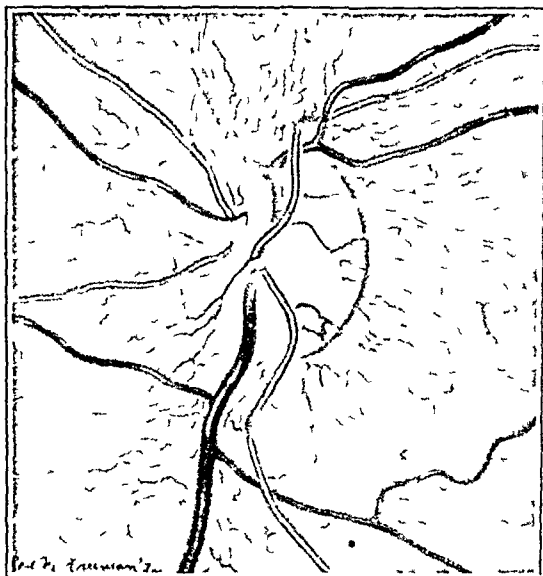


Fig 6—Hypertension with beginning arteriolar sclerosis. The general caliber of the arteries in this case was normal, but there were some local constrictions on the inferior branch which appeared and disappeared during the examination (spasm). The arterial walls were visibly thickened at some places, and the arterial light streak showed increased brightness. Arteriovenous compression was observed at only a few vascular crossings (outside the area represented in the drawing).

The patient, a white woman aged 31, had hypertension of nine years' duration and a blood pressure of 240 systolic and 140 diastolic at the time of examination. She had had bouts of hematuria at intervals for seven years, toxemia of pregnancy and a therapeutic abortion eight months before the examination. The urine gave a 1 plus reaction for albumin, but responses to the phenolsulfonphthalein and concentration tests were normal. She died in uremia four years after this drawing was made.

Some of these questions are approachable through the study of experimental atherosclerosis. It is much to be regretted that interest in this field of research, after an enthusiastic beginning, has lapsed. But there are many questions for which no experimental short cut exists and which can be solved only by the slow and painstaking extension of ophthalmoscopic, general clinical and pathologic correlations.

The Hypertensive Arteriosclerotic Process—This is the field in which the greatest advances have been achieved during the past decade Goldblatt and associates⁶ demonstrated that renal ischemia in dogs results in severe hypertension, generalized arteriolar sclerosis and progressive renal failure. A number of independent investigators have shown that the disease depends on a humoral factor liberated by the ischemic kidney. The complex nature of the humoral mechanism need not be discussed here. What is of importance is the fact that the malignant phase of hypertensive disease, as defined by Volhard, bears the closest possible resemblance to the experimental disease produced by Goldblatt.

The malignant phase is, in all but the most exceptional cases, preceded by a phase of "benign" hypertension, which may last for many years. The clinical transition from the benign to the malignant phase is generally rather abrupt. Histologic and ophthalmoscopic studies in the later portions of the "benign" phase reveal that hyaline degeneration of the arteriolar walls has already appeared, and the transition from the "benign" to the malignant phase seems to be more a quantitative than a qualitative one, though in the severest forms arteriolar necrosis is added to the previous arteriolar hyaline degeneration.

It has already been pointed out that in patients with atherosclerosis and hypertension renal involvement and arteriolar hyaline degeneration can also develop and the disease thus enter a malignant phase in many respects similar to that which complicates essential hypertension. These two disease processes consequently present many external similarities. To what extent can they be differentiated from one another? To what extent can ophthalmoscopy contribute to the differential diagnosis?

The answers to these questions are by no means simple, and the differential diagnosis in many cases remains unsharp. Age distribution assists in distinguishing many cases. Most patients with atherosclerotic hypertension are over 60, and few are under 50. Most of the patients with nonatherosclerotic essential hypertension have the onset of their hypertension under the age of 50 and have well developed signs of arteriolar hyaline changes in the retinal vessels before they reach 60. Thus, patients under 40 or over 60 years of age present no serious difficulties in the differential diagnosis of these forms. But the age group of 40 to 60 forms an important fraction of the patients for whom the differential diagnosis needs to be made.

⁶ Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W. Studies on Experimental Hypertension. I. Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, *J. Exper. Med.* **59** 347, 1934. Goldblatt, H. Studies on Experimental Hypertension. V. Pathogenesis of Experimental Hypertension Due to Renal Ischemia, *Ann. Int. Med.* **11** 69, 1937.

It is often said that in patients with atherosclerotic hypertension the diastolic blood pressure shows little, if any, rise and that this feature differentiates atherosclerotic from essential hypertension. This asser-

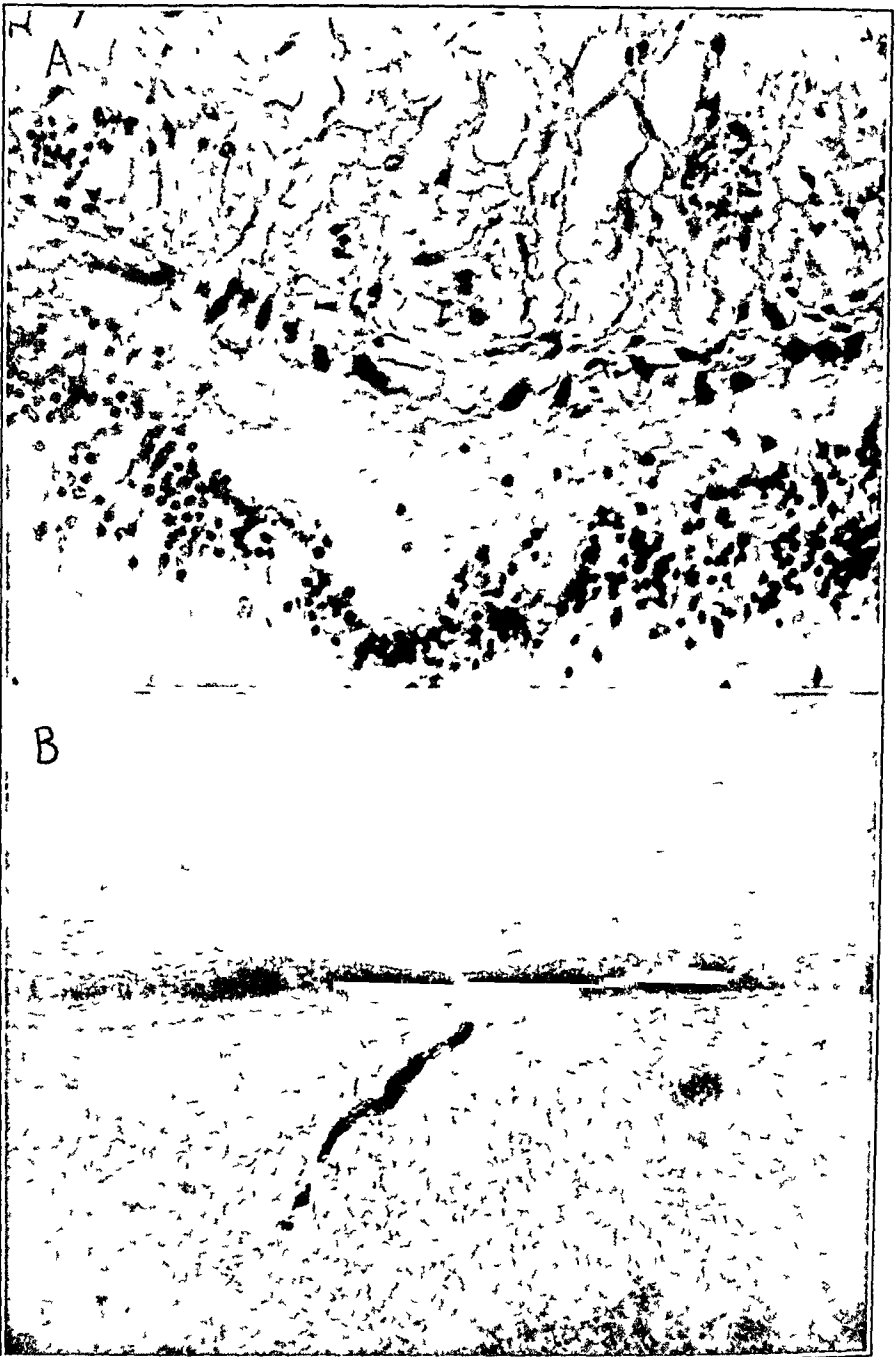


Fig 7—*A*, hyaline arteriolar sclerosis, *B*, flat preparation stained for fat, showing hyaline arteriolar sclerosis. Note that the large vessel, which is of the same order of magnitude as that shown in figure 3, has a diffusely thickened, highly refractile wall, while the smaller branch shows, in addition lipid infiltration

tion, however, confuses the atherosclerotic process with the senile loss of arterial elasticity, with which it is often associated. Elderly people with normal diastolic pressures but large pulse pressures are not really hypertensive, and they do not contribute to the problem of differential diagnosis which I am now discussing. The group whose condition I have designated as atherosclerotic hypertension consists mainly of elderly people with fixed hypertension. When the disease is well established in these persons, the pressures range from 180 to 220 systolic and from 100 to 120 diastolic.

If one is to use the ophthalmoscope in assisting in the differential diagnosis of hypertension in middle-aged persons, one must first analyze the findings in those age groups in which the differential diagnosis is unconfused. In patients over 60 with moderate fixed hypertension, the retinal vessels are almost always narrow and straight and branch at acute angles. The relation between the degree of arterial narrowing and the degree of hypertension is close. With systolic pressures in the neighborhood of 160, the narrowing is usually just barely perceptible. When the systolic pressure has reached 200, the arteries are reduced to about one-half the diameter of the veins. The correlation between blood pressure and arterial caliber in this group of patients is so close that one can usually guess the pressure rather accurately from the ophthalmoscopic examination. The correlation is, in fact, so close that if an elderly patient does not have as high a blood pressure as the degree of narrowing of the retinal vessels suggests serious consideration should be given to the possibility that an intercurrent disease has lowered the blood pressure below its compensated level.

In patients under 40 with essential hypertension, the retinal arteries are generally of normal caliber and tortuosity. If constriction occurs at all, it is usually segmental or involves only isolated branches, rather than the whole arterial tree. Even when, in the exceptional case, generalized diffuse constriction is present, the degree of constriction is almost always less than that seen in elderly patients with the same amount of hypertension. This description refers specifically to the early stages of the hypertensive disease before extensive hyaline thickening of the retinal arterial walls has taken place. When the hyalinization is well developed, the arterial blood column is often narrow, though the vessel commonly remains tortuous.

With these distinctions in mind, what light can be thrown on the differential diagnosis of hypertension in the middle-aged patient? If the retinal arteries show obvious evidence of hyaline thickening, on the one hand, or of atheromatous plaques, on the other, no serious diagnostic difficulty remains, but if one must be guided merely by observations on caliber and tortuosity, one can do no more than guess. In these circumstances, if the retinal arteries are of normal caliber and

tortuosity, the diagnosis of essential hypertension seems most likely. The same conclusion is to be drawn if the blood pressure is much higher than the degree of arterial narrowing would suggest. On the other hand, if the degree of narrowing of the retinal arteries is proportionate to the hypertension in the sense previously outlined, the case probably belongs to the atherosclerotic group.

Whatever the final decision in this difficult diagnostic problem, the fact remains that in young hypertensive patients there is much less correlation than in elderly hypertensive patients between the degree of the hypertension and the degree of constriction of the retinal arteries. The occurrence of hypertension without constriction of the retinal arteries raises interesting hemodynamic problems. So far as the retinal arterial tree may be taken as a guide, the vascular obstruction in cases of this type would appear to be farther downstream—close to the capillaries—than in cases in which the ophthalmoscopically visible branches are narrow.

As the essential hypertension progresses from the "benign" toward the malignant stage of the disease, the hyaline arteriosclerotic process can be observed in its purest form. There is an increased thickness of the arterial wall fairly diffusely distributed over the whole retinal arterial tree, but often more pronounced in some portions than in others. The thickening of the vessel walls can often first be suspected when there is an increased brightness and width of the arterial light streak, giving the vessel a coppery appearance. This particular ophthalmoscopic sign is one about which many observers find it difficult to be objective. Moreover, the width and brightness of the vascular light streak are greatly influenced by the size of the pupil and by the illuminating system of the ophthalmoscope. A more reliable sign of thickening of the arterial wall is the separation of the arterial and the venous blood columns at the points of their crossing. This manifests itself in an indentation of the vein when it lies under the artery and a knuckling forward of the vein when it lies over the artery.

With the best resolving power in the ophthalmoscope, the hyalinized vessel walls often become visible as a glassy coat surrounding the blood column. Those who have used the slit lamp hand ophthalmoscope will be familiar with the fact that by focusing the image of the illuminated slit close to, but not on, a retinal vessel, and thus illuminating the vessel with light reflected from the choroid, the surface of the vessel wall becomes visible as a glassy cylinder. By comparing the diameter of the vessel wall made visible in this way with the diameter of the blood column on direct illumination, a fairly reliable estimate of the thickness of the vessel wall can be reached. The unevenness of the process of hyalinization often leads to localized variations in the width of the blood

column. Often these localized narrowings are associated with rather sharp right angle bends in the vessel.

As the malignant phase of the disease is approached, hemorrhages and cotton wool spots appear. The hemorrhages are most often flame shaped but may be petechial. The cotton wool spots are often spoken of as exudates, but this is a misnomer. The great majority of these fluffy, opaque lesions are focal necroses in the superficial layers of the retina, and on section are seen to be composed of swollen dead cells, presumably glial cells, lying between the bundles of nerve fibers. These are the "cytoid bodies," about which there is an extensive histologic literature. The hemorrhages and cotton wool spots commonly appear in crops. Often their appearance is associated with a sudden exacerbation of the blood pressure. The individual hemorrhages and cotton wool spots usually disappear in a few days or weeks, and if fresh lesions do not develop pronounced improvement in the ophthalmoscopic appearance may take place. Such apparent spontaneous remissions of the disease are common, and great care must be exercised in using the short range course of the ophthalmoscopic picture as an index to interpretation of the effect of a therapeutic procedure.

At a still later stage, neuroretinal edema, with a star-shaped figure in the macula, flat detachment of the retina, and other changes appear. The edema is commonly regarded as the sign of transition from the "benign" to the malignant stage of the disease. However, spontaneous remissions can still occur, even after the appearance of neuroretinal edema. Moreover, as Goldring and Chasis⁷ pointed out, an appreciable minority of patients go into the malignant stage and die in uremia without ever having had neuroretinal edema. In order to test the correlation between retinal and renal hyaline arteriolar sclerosis, I studied the kidneys of 20 patients with neuroretinal edema who showed the most extensive hyaline changes in the retinal arterioles. Every kidney showed some glomerular afferent arterioles that were hyalinized, but the extent of the lesion varied from very mild to very severe. Similarly in a series of 20 patients showing the severest hyaline arteriolar sclerosis in the kidney every retina showed some similarly affected vessels, but the extent of the lesion varied from very mild to very severe. Moreover, the hyalinization of the arterioles takes some time, and one occasionally observes in cases of the most fulminating type neuroretinal edema, focal necroses, hemorrhages and exudates without appreciable hyaline changes in the retinal arterioles. This is almost regularly the picture case in cases of fatal eclampsia. It may, however, be argued that eclampsia and malignant hypertension are not identical.

⁷ Goldring, W., and Chasis, H. Hypertension and Hypertensive Disease, New York, The Commonwealth Fund, 1944, p. 28.

In many cases of the severe form of the disease, arteriolar necrosis occurs in the retina as well as in the kidney and other organs. Then the endothelium, as well as the media, becomes converted into a structureless hyaline mass, and a fibrinous clot fills the lumen. On ophthalmoscopic examination such vessels appear as white, bloodless cords. However, not every such "silver wire" vessel is necrotic and occluded, for sometimes the hyalinized wall becomes opaque and hides the blood column in one region, though the vessel may still be patent and the blood column still visible in the more terminal portions.

In cases of the atherosclerotic type the approach to the malignant stage of the hypertensive disease is accompanied with a similar development of hyaline sclerosis in the retinal arterioles, complicated, in these cases, by the preceding, and progressive, atheromatous lesions. In these cases the retinal arterial tree generally remains narrow and straight even when the hyaline process has come to predominate in the picture. Often localized atheromatous plaques are seen. Major vascular accidents—arterial and venous occlusions—occur as they do in cases of atherosclerosis in the absence of hyaline arteriolar sclerosis. Sometimes the same branch shows simultaneously the two types of lesions.

In general, the rate of downward progress in the atherosclerotic group is slower, and the duration of the phase of "benign" hypertension longer, than in the nonatherosclerotic group, but this is not invariably the case. Moreover, in many cases of the atheromatous type the malignant stage of the hypertensive disease never develops, but the patient dies instead of a cerebral or cardiac vascular accident or other intercurrent disease. However, the transition to the malignant phase, and the consequent association of atheroma with hyaline arteriolar sclerosis are sufficiently frequent to lead over and over again to confusion about their interpretation. The ancient error is still repeated that atheroma and hyaline degeneration represent the same disease process, differing only in the size of the vessel affected. The fact that these two lesions can be produced experimentally, each in quite pure form, by different and unrelated experimental procedures is solid evidence that the two processes are distinct. Conclusive evidence, however, is found in the retinal vessels, for in retinal arterial branches of the same size and anatomic structure, atheromas may develop in one and hyaline degeneration in another, depending on the nature of the systemic condition. Indeed, when both processes are present, the same retinal vessel can exhibit both lesions.

In the section on atherosclerosis, the mechanism was discussed by which the atheromatous process can lead to malignant hypertension and hyaline arteriolar sclerosis. The role of atheromas of the renal arteries in bringing about this complication has been widely considered in the literature and need not be discussed here. The reverse process, whereby

primary hyaline arteriolar sclerosis might lead to atheroma as a complication, requires comment. It is a familiar fact that some young patients with essential hypertension die of coronary occlusion or cerebral apoplexy, instead of malignant hypertension and uremia. Dr Alfred Cohn, many years ago, showed me serial sections of the occluded regions in coronary arteries in which he had noted, in the media of the affected vessels, occluded hyalinized arterioles of the vasa vasorum. These observations suggest a possible mechanism whereby, in cases of hyaline arteriolar sclerosis, atheromatous plaques and occlusions of major arteries may develop as complications.

In summary, the course of the hypertensive arteriolosclerotic disease complex can be followed reasonably closely with the ophthalmoscope, though the correlation is not an absolute one. Spontaneous remissions occur in relation to retinal hemorrhages, cotton wool spots and neuroretinal edema, and this must constantly be kept in mind in evaluating supposed therapeutic benefits. Patients in the "benign" phase of hypertensive disease can be divided into two distinguishable groups, which differ from one another not only in their ophthalmoscopic pictures but also in their age incidence and clinical course. Arguments have been presented for regarding one of these groups as primarily atherosclerotic and the other as nonatherosclerotic. I have been unable to find in the literature concerning various therapeutic attempts any clear analysis of the therapeutic results in these two groups considered separately. Perhaps this is because the distinction is of no significance in relation to therapeutic results, perhaps because the same distinction has been achieved by consideration of wholly other criteria. It is generally agreed, for instance, that sympathectomy is not to be recommended for patients over 50, the majority of hypertensive patients with narrow, straight retinal arteries being thus automatically ruled out.

Diabetic Vascular Lesions of the Retina—In the divisions of the subject discussed in the preceding sections, the important recent advances in knowledge have come from outside the domain of ophthalmology. In the division which I have saved for last, the recent contributions have come chiefly from ophthalmologists. The thorough clinical studies of Waite and Beetham⁸ and of Hanum⁹ revealed that diabetic retinitis is related much more closely to the duration of the diabetic disease than to its severity. Since diabetic patients under modern care live longer than they did before the use of insulin, the frequency of this complication is increasing. The most careful regulation of the blood sugar seems to

⁸ Waite, J. H., and Beetham, W. P. Visual Mechanism in Diabetes Mellitus, *New England J. Med.* **212** 367 and 429, 1935.

⁹ Hanum, S. Diabetic Retinitis. Clinical Studies of One Hundred and Ninety-Five Cases of Retinal Changes in Diabetics, Copenhagen, Einar Munksgaard, 1939.

have little effect in preventing the onset of the retinitis, and no effect at all in preventing the progress of the retinitis once it is well established

When minute retinal petechiae occur in other diseases, they are regularly absorbed in a few days. The petechiae of diabetic retinitis, however, persist for months, as was first shown conclusively by photographic studies. Balantine and Loewenstein¹⁰ have recently demonstrated that the petechiae are often surrounded by an endothelial

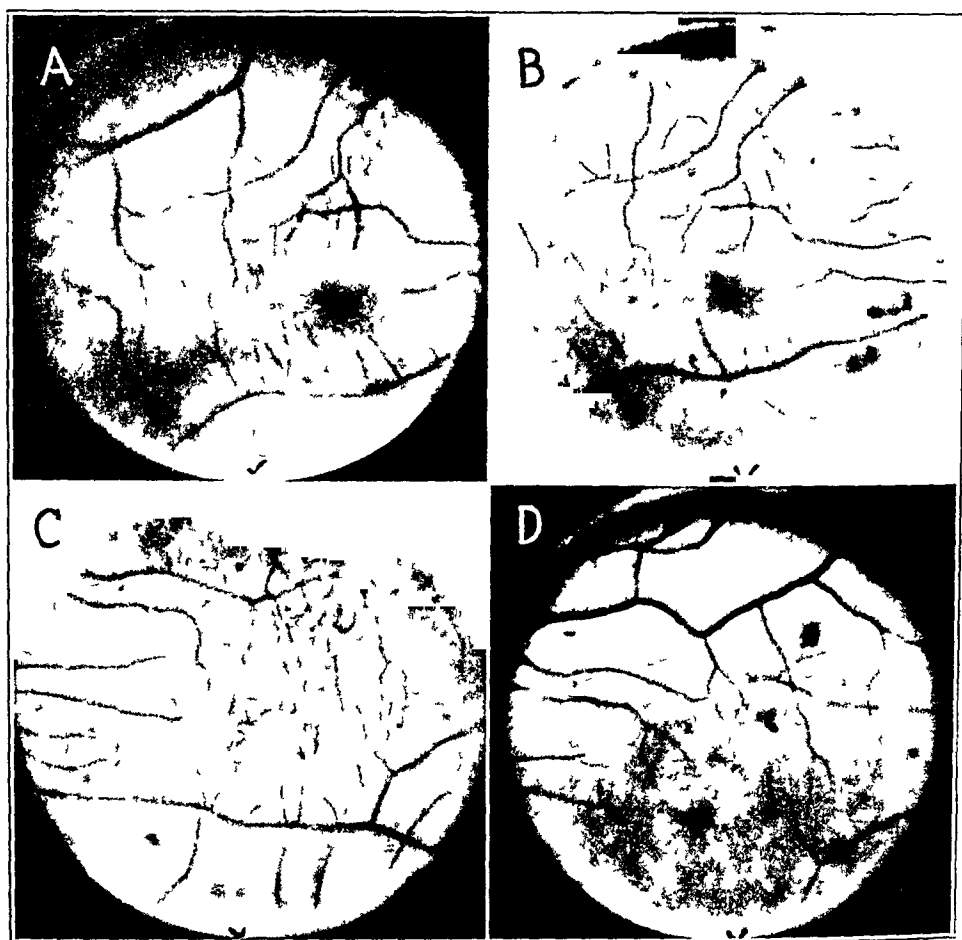


Fig 8—*A*, diabetic retinitis, *B*, appearance of the fundus in the same case ten weeks later, *C*, diabetic retinitis in another case, *D*, fundus in the same case ten weeks later

sac and actually constitute small saccular aneurysms connected with capillaries. I can confirm these observations and, in addition, can report that the aneurysmal sacs are often incompletely lined with endothelium. This indicates that the leakage of blood occurs first, and that the endothelium grows out to cover it afterward. Both the

¹⁰ Balantine, A. J., and Loewenstein, A. Retinal Micro-Aneurysms and Punctate Haemorrhages, *Brit J Ophth* 28 593, 1944

initial persistence of the petechia and its subsequent enclosure by an outgrowth of endothelium suggest that the process develops from a break in the capillary wall, leading to a persistent slow leak of corpuscles. The hole in the wall evidently shows little tendency to heal. Instead, the endothelial cells grow out around the mass of extravasated red cells, eventually forming a minute saccular aneurysm.

If this explanation of the hemorrhages is correct, the accompanying hard white exudates can probably be explained as the consequence of still smaller breaks in the capillary wall through which plasma, but no red cells, escape. The deposit of plasma proteins in the retinal



Fig 9—Diabetic retinitis, showing a capillary opening into a partially endothelialized hemorrhage

tissue spaces and the inspissation of this deposit as the water filters back into the vascular system would explain the extremely high protein content of these exudates, a feature which distinguishes them from the serous extravasations associated with the neuroretinal edema of malignant hypertension. The photographic studies of Bedell¹¹ have demonstrated that exudates in diabetic retinitis are not derived from hemorrhages, as was previously thought.

It is difficult to obtain conclusive histologic evidence for the possible course of events here outlined, but indirect evidence is furnished by the

¹¹ Bedell, A. Fundus Changes in Two Hundred and Five Diabetics, *Tr Ophth Soc U Kingdom* (pt 1) 59 219, 1939

report of Hanum⁹ that patients with diabetic hemorrhagic retinitis show increased capillary fragility. I can confirm these observations. The simplest, and for these cases the most reliable, test of capillary fragility is performed by placing a blood pressure cuff around the upper part of the arm and inflating it to a pressure of 100 mg of mercury for three minutes, or to a pressure of 80 mm of mercury for five minutes.

After the cuff is removed, the arm is held elevated for a few moments to relieve the congestion and to make the petechiae stand out more sharply. Normal persons show no petechiae or at most twenty to thirty. If more than fifty petechiae develop, the test is certainly positive.

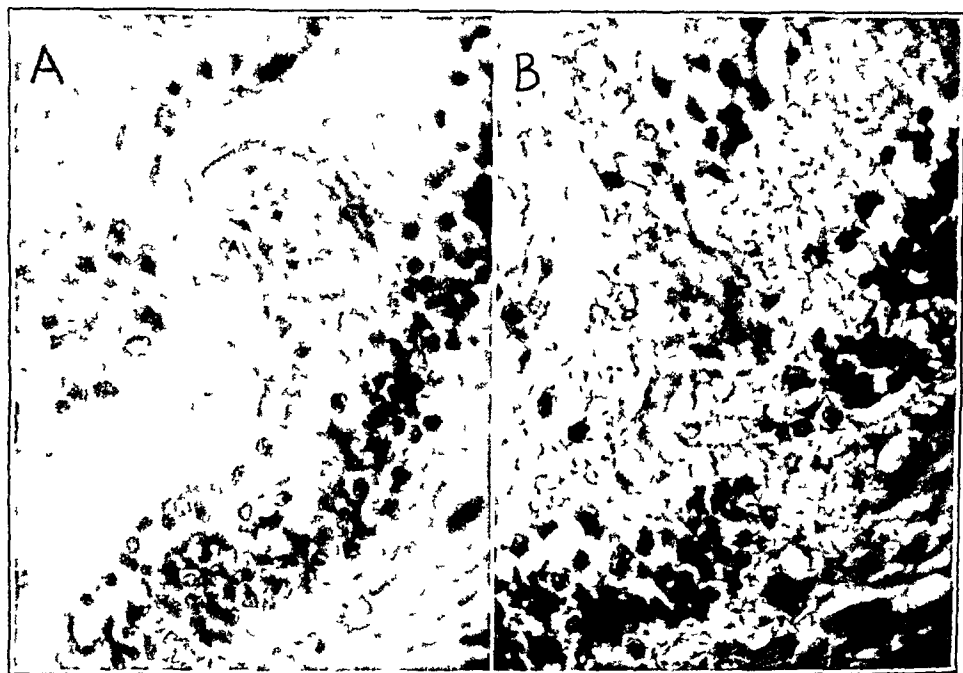


Fig 10—Diabetic retinitis. *A*, capillary and adjacent hemorrhage, *B*, adjacent serial section, showing connection between the capillary and the hemorrhage.

Many patients with diabetic retinitis tested in this way show innumerable petechiae not merely in the antecubital fossa but on the wrist and the dorsum of the hand. In my experience, all patients with diabetic retinitis exhibit more petechiae than the average normal subject, though some are within the normal range. The vascular stasis and cyanosis produced by this method of testing for capillary fragility appear to facilitate the development of a positive response in these patients, for the suction test for capillary fragility, which is generally regarded as a more refined method, while confirming the results with the pressure cuff, does not reveal quite so sharp a distinction between patients with diabetic retinitis and the normal controls. The results for diabetic patients without retinitis tested by either method fall within

the normal range. There seems to be no doubt that the retinitis is a manifestation of a general capillary abnormality. How this abnormality is related to the metabolic disturbance of the diabetic patient is still a mystery.

It might be supposed that postmortem studies of the viscera of diabetic patients would throw light on the condition of their capillaries. Unfortunately, I must report that in my hands such a study has been unavailing. I have searched microscopic sections of the viscera of 10 diabetic patients with retinitis, comparing them with the viscera of 10 diabetic patients without retinitis but of approximately the same ages. All 20 patients showed numerous petechial hemorrhages in the viscera, and no difference could be seen between those with retinitis and those without retinitis. Furthermore, patients do not nowadays die of diabetes. Diabetic persons die of infectious diseases, surgical shock, carcinoma or other intercurrent disease, all of which are associated with petechial hemorrhages in the viscera as a terminal event. It is therefore extremely difficult to find autopsy material devoid of such complications. It would seem that one must wait for the experimental production of diabetic retinitis for a deeper attack on its pathogenesis.

The relation of diabetic retinitis to atherosclerosis has long been the subject of discussion. Before insulin was available, all juvenile diabetic patients died after a relatively short illness. Consequently, diabetic retinitis was seen almost exclusively in elderly persons and was usually associated with evidence of generalized atherosclerosis. With modern treatment, cases of juvenile diabetes have appeared in increasing numbers, and in many of these there are no recognizable clinical signs of atherosclerosis. Among the 10 diabetic patients with retinitis in the postmortem study reported in the preceding paragraph was 1 who died at the age of 26 and who had shown no clinical signs of atherosclerosis. The aorta of this patient, however, did show small atheromatous plaques, and none of the other 9 patients were completely free from similar lesions. The importance of this observation, is, however, open to debate, for the question is not whether a sclerotic plaque exists in some remote organ but whether local atherosclerosis in the retina is responsible for the retinitis. The answer to this is unequivocally "no." Many patients are seen clinically without any signs of sclerosis in the ophthalmoscopically visible vessels. I have studied serial sections of the eyes of several such patients without seeing any evidence of atherosclerosis of the retinal vessels. Though the unknown systemic condition which produces atheroma may perhaps be present in all patients with diabetic retinitis, as indeed it is in practically all persons beyond youth, the retinal vessels in many patients show no lesions other than the capillary aneurysms. The only valid question, therefore,

is whether the capillary disturbance in these persons is itself an atherosclerotic manifestation

The answer to this question is complicated by the fact that some elderly persons with obvious atherosclerosis and without diabetes show petechial retinal hemorrhages and hard white spots of exudate similar to those seen in diabetic patients. H. Friedenwald¹² reported many years ago that approximately one third of the patients presenting this ophthalmoscopic picture failed to show glycosuria. This was before the days of blood sugar measurements and sugar tolerance tests, and it may be that some of the patients without glycosuria had, in fact, mild diabetes. Even with modern methods of testing, however, a small group of nondiabetic patients remain. The nature of the retinal lesions in these nondiabetic patients has not been studied histologically, but there is one clinical feature that serves to distinguish them from true diabetic retinitis. The individual petechial hemorrhages in these patients persist only a few days, instead of months, as in the diabetic patient. It seems likely, therefore, that the pathologic process is different, however closely the ophthalmoscopic picture may resemble that of diabetic retinitis. There is, therefore, little evidence remaining to support the hypothesis that diabetic retinitis is an atherosclerotic manifestation.

The course of diabetic retinitis is in general progressive, but careful studies with repeated photographs of the fundus reveal the fact that there may be many months between the appearance of fresh lesions. Moreover, the individual petechiae and exudates eventually disappear, even though months are required for this to happen. If these patients are examined frequently over long periods in the early stages of the disease, spontaneous remissions can almost always be observed, and this must be borne in mind in evaluating therapeutic results.

COMMENT

The effort to account for differences in ophthalmoscopic interpretation of retinal vascular disease and for discrepancies between ophthalmoscopic and general clinical diagnoses has necessarily been a discursive one. I hope that this has not obscured some conclusions which seem to me quite clear.

1 For the most part, what one sees of the retinal vascular tree is the blood column of the larger vessels. Conclusions as to the functional and histologic processes in the vessel walls based on observations of the blood column are necessarily inferential and subject to error and dispute.

2 The basic processes which affect the vascular tree which are potentially independent disease entities and which can occasionally be

12 Friedenwald, H. Retinitis Diabetica, Arch. Ophth. 20: 544, 1891

observed in pure, uncomplicated form, are also, in varying degrees, potentially interrelated, so that the combined occurrence of several different processes is frequent. The hypotheses which have been presented here as possible explanations of these interrelations and as possible ways of accounting for the frequent existence of impure and complicated cases, are presented as a framework for the ordering of ideas, not as final conclusions. Evidence of varying weight supports them, but they are as yet unproved.

3 In every aspect of the subject there are problems awaiting attack by methods already available. At no time in the last twenty years has the subject of retinal vascular disease presented more enticing opportunities for clinical, pathologic and experimental study.

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AIMS AND AIDS IN THE TEACHING OF BASIC SCIENCES IN OPHTHALMOLOGY

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STUDY of the basic sciences as applied to the eye gives promise of becoming a regular part of the prospective ophthalmologist's training. Some institutions already require such a study before accepting a candidate for a clinical residency, presumably, an increasing number of others will do so in the future. In the belief that experience in organizing and conducting such a course at the Harvard Medical School may be of use to others, the aims of the course as it is now given and certain of the laboratory technics which have been found most practicable¹ are presented in this paper. The writing of it has been prompted by inquiries from those who are proposing to set up basic science courses in ophthalmic institutions elsewhere.

AIMS

A basic science course in ophthalmology should aim primarily to lay a foundation for the appreciation of clinical ophthalmology. It should be to the ophthalmic education at the graduate level what the preclinical subjects in the medical school, usually those of the first two years, are to the general medical education at the undergraduate level. Just as it is important for the medical school student to devote a considerable portion of his time to the study of the basic subjects, it behooves the prospective ophthalmologist to spend whatever time is necessary to learn the application of these subjects to the organ that is to be the basis of his professedly specialized knowledge. Moreover, a course in the basic sciences at the graduate level not only should provide fundamental knowledge about the eye but, what is of equal importance, should also generate a set of standards and a critical judgment by which the student may properly evaluate clinical and laboratory work.

The basic science course bridges the field of general medicine and the specialty of clinical ophthalmology. In no other specialty are there such disciplines required in what may be called the borderlands of

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¹ The course has been developed with the assistance of Henry Allen, M D, Russell Carpenter, Ph D, W Morton Grant, M D, V Everett Kinsey, Ph D, Sumner Liebman, M D, and Elek J Ludvigh, Ph D.

medicine Physical optics is one example, the complex fields of stereopsis, accommodation and transmissibility of various types of radiant energy are others Then there are fields which may be touched on in the general medical curriculum but should be elaborated for the prospective ophthalmologist Examples are the visual purple mechanism in the retina, osmotic forces in the cornea and fluid movement across the blood-aqueous barrier, to mention but a few These subjects have little significance for the average medical trainee, but for the ophthalmologist they merit special study

Some eager persons, to be sure, will obtain adequate training without a course Organized training can offer to these persons only a more efficient means of obtaining the information But it is not for them that the courses are primarily intended It is for the average person who is to take a clinical internship and who will otherwise get only a superficial knowledge of the basic sciences

The success of the course must depend in large measure on the faculty While a sympathetic administration is desirable and adequate space is practically essential, it is nevertheless the teachers who will make or break the course Too often in postgraduate teaching, as in other affairs, the organization is set up and the teaching staff is taken for granted This is because the courses are set up by organizers and not by the teachers themselves Emphasis should be put on the teachers and the course organized about their qualifications This is accomplished in practice by allocating time according to what the teacher has to offer To omit a subject is less of an evil than to have it taught poorly

The following subjects as applied to the eye and the percentage of time allotted to each are suggested as a tentative schedule, to be varied according to the teaching capabilities available Pathology is incorporated with the clinicopathologic course which follows the basic course and is therefore not listed in the following schedule

	Percentage
Anatomy, histology and embryology	23
Physical and physiologic optics	23
Physiology and biochemistry	19
Neuroanatomy and neurophysiology	18
Bacteriology	8
Pharmacology and toxicology	4
Ophthalmic instrumentation	4
Miscellany (heredity, electroencephalography)	1

It is best that the teaching of these specialized subjects be done by persons who are actively working in the field of ophthalmology Such persons are to be found almost exclusively in ophthalmic research centers The teaching should not be farmed out indiscriminately to members in the basic science departments in the medical school who have had no special interest in the eye nor to clinicians who have had little

contact with the basic sciences. In so far as there are few ophthalmic centers at present having the personnel trained in the basic sciences, the courses, at present, should be given in only a limited number of places. The classes should be sufficiently large, however, to supply the residents for the many clinical institutions which do not have the basic science facilities.

The course should be taken by a student just prior to his ophthalmic residency if possible, but in any case not during the residency. Since much study and freedom of mind are required, it is inadvisable to mix clinical work with the basic studies, especially when the preoccupying duties of a house officership are involved. The duration of the pre-clinical course should be a minimum of twelve weeks' full time study, approximately one half of the classroom time should be laboratory exercises.

AIDS

It is the purpose of this section to describe some demonstrations and experiments which have been found especially useful in the students' laboratory sessions. Since much of the laboratory work in ophthalmic basic science courses is new, most of the exercises here described have been developed *de novo*. It would be helpful if other instructors would similarly report their teaching aids as developed.

The laboratory work in anatomy consists of dissection of the human orbit (not more than two men to an orbit) and the gross dissection of beef eyes. In embryology and histology, it consists of microscopic study of slide material prepared from animal and human eyes. The sections from human eyes are prepared as serial cross sections of the globe, stained at regular intervals with different dyes to show the various histologic structures and yet permit reconstruction of the whole eye.

The laboratory work in physiology revolves about the following subjects: corneal permeability and corneal swelling (experiments similar to those previously described)², permeability of the blood-aqueous barrier as determined by transfer of fluorescein into the eye and the effects of various drugs on it, mechanism of aqueous humor formation, as determined by vital staining of the ciliary process³ and transfer of ascorbic acid into the eye⁴, effect of ultraviolet radiation on the cornea.

2 Cogan, D. G., and Kinsey, V. E. The Cornea. I. Transfer of Water and Sodium Chloride by Osmosis and Diffusion Through the Excised Cornea, *Arch Ophth* **27** 466-476 (March) 1942, The Cornea. III. Hydration Properties of Excised Corneal Pieces, *ibid* **28** 272-284 (Aug.) 1942, The Cornea. IV. Hydration Properties of the Whole Cornea, *ibid* **28** 449-463 (Sept.) 1942.

3 Friedenwald, J. S., and Stiehler, R. D. Circulation of the Aqueous. VII. A Mechanism of Secretion of the Intraocular Fluid, *Arch Ophth* **20** 761 (Nov.) 1938.

4 Kinsey, V. E. To be published.

and of infra-red radiation on the whole eye⁵, measurement of reducing substances in the lens and of vitamin A in the retina, determination of the absorption spectrums of vitamin A and visual purple with the spectrophotometer, measurement of the accommodative power of the eye (Scheiner's experiment) and of the size of the pupil (objective and entoptic methods), production of experimental glaucoma in the rabbit by ligation of the vortex veins, and observations on autokinetic ocular movements and artificially produced nystagmus (rotatory and caloric stimuli)

The laboratory work in physical and physiologic optics consists of standard optical bench procedures, using a somewhat modified bench,⁶ dark adaptation studies, critical flicker frequency measurements, horopter determinations and after-image studies

The laboratory work in neuro-ophthalmology includes the following exercises—construction of a model eye out of a golf ball⁷ to illustrate the mechanics of extraocular muscle action, construction of a brain model⁸ showing the ocular motor centers in the brain stem and the visual pathways, drawing of cross sections and longitudinal sections of the brain stem through the third, fourth and sixth cranial nerve nuclei, drawings of the base of the brain, and study of the excellent stereoscopic drawings of the brain prepared by Leinfelder and Allen⁹

In bacteriologic exercises, the students are instructed in the technics of taking and preparing conjunctival smears and scrapings, including standard stain and culture methods. They are given prepared culture plates of organisms commonly encountered in ophthalmology and are required to describe the colony and cytologic characteristics of the various types of bacteria, similarly, they are held for a description of inclusion bodies and fungi assigned to them. Finally, they are given preparations illustrating the actions of several antibiotics and of anti-antibiotics

The laboratory work in ophthalmic instrumentation is necessarily varied. Slit lamp biomicroscopy begins with exercises on adjustment and measurement of magnification. Then the student examines with the instrument special optical chambers¹⁰ made to simulate the eye, containing various fluids illustrating the appearance of colloids, particulate matter, blood cells and convection currents. The types of illumination

5 Cogan, D. G., and Kinsey, V. E. Action Spectrum of Keratitis Produced by Ultraviolet Radiation, *Arch. Ophth.* **35** 670-677 (June) 1946

6 Ludvig, E. J. To be published

7 Cogan, D. G. To be published

8 Liebman, S. D. A Model of the Visual Pathways, *Arch. Ophth.* **27** 1122-1125 (June) 1942

9 Leinfelder, P. J., and Allen, L. Unpublished data

10 Grant, W. M. To be published

and structures to be visualized are determined first on the enucleated beef eye and then on the living rabbit eye, with the introduction of such experimental variations as vital staining of corneal nerves and the production of epithelial edema. Finally, the characteristics of the normal human eye are determined by having the students examine each other.

Ophthalmoscopy, direct and indirect, is practiced by the students first on models and then on each other, with the introduction of such variables as color and polarizing filters. Dynamometry is practiced, and the students are asked to compare the diastolic pressure of the retinal arteries with that of the brachial artery. After the angle of the anterior chamber in beef, rabbit and human eyes is examined as far as possible with the slit lamp biomicroscope, various gonioscopic techniques are tried, first with a small right angle prism¹¹ and subsequently with standard contact lenses.

Various types of tonometers (Maklakov, Schiøtz and Souter) are used on animal eyes and on the eyes of fellow students with exercises illustrating the advantages and limitations of each. Finally, exercises are prescribed illustrating the routine procedures in perimetry, campimetry, stereocampimetry and angioscotometry.

Laboratory outlines are given the students to guide them in the foregoing exercises and one or more instructors are always in attendance to volunteer suggestions and to answer questions, but every effort is made to have the student derive his own answers and to reach an independent judgment. It is felt that in this way only will he obtain the measure of self confidence and independence of judgment that is as important as the knowledge derived from the specific experiments themselves.

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¹¹ Grant, W. M. Unpublished data.

PRIMARY LIPID DYSTROPHY OF THE CORNEA

ALAN DAVIDSON, M D

DURHAM, N C

DYSTROPHIA adiposa corneae was first described by Kamocki¹ in 1893 in a paper entitled, "A Case of Fatty Degeneration of the Cornea with Intermittent Irritative Phenomena" Katz and Delaney,² in their careful review of the cases reported up to 1933, found only 8 undoubted instances of primary fatty degeneration of the cornea. These cases were reported by Kamocki¹ (Warsaw), 1893, Tertsch³ (Vienna), 1911, Bachstetz⁴ (Vienna), 1921, Kusama⁵ (Tokyo), 1921, Verderame⁶ (Turin), 1922, Elschmig⁷ (Prague), 1923, Denti⁸ (Milan), 1926, and Meyer⁹ (Freiburg), 1928. Katz and Delaney also recorded a list of 7 cases that they felt did not fulfil the narrow limits of the condition, in that all occurred shortly after an ocular inflammation. These cases were reported by Takayasu¹⁰ (Japan), 1912, Dor¹¹ (France), 1913, Meesmann¹² (Berlin), 1928, Spanlang¹³ (Vienna), 1927, and Gilbert¹⁴ (Hamburg), 1929. A search of the literature since 1933 has revealed only 3 cases reported as instances of primary fatty dystrophy: a case reported by Katz and Delaney² (Chicago), 1933, and 2 cases by Wright¹⁵ (India), 1936.

From the Ophthalmological Division, Surgical Department, Duke Hospital and Medical School

1 Kamocki, V. Arch f Ophth **39** 209, 1893

2 Katz, D, and Delaney, P. A. Dystrophia Adiposa Corneae, Arch Ophth **9**:78 (Jan) 1933

3 Tertsch, R. Klin Monatsbl f Augenh **49**.1, 1911

4 Bachstetz, E. Arch f Ophth **105** 997, 1921

5 Kusama. Klin Monatsbl f Augenh **66** 111, 1921

6 Verderame, cited by Clausen, W. Zentralbl f d ges Ophth **10** 56, 1923

7 Elschmig, H. H. Klin Monatsbl f Augenh **71** 720, 1923

8 Denti, cited by Rohrschneider, W. Zentralbl f d ges Ophth **18** 49, 1927

9 Meyer, H. Klin Monatsbl f Augenh **81**.786, 1928

10 Takayasu, M. Arch Ophth **82** 475, 1912

11 Dor, cited by Gebb. Jahresb u d Leistung d Ophth **44**.388, 1913

12 Meesmann, A. Die Mikroskopie des lebenden Auges, Berlin, Urban & Schwarzenberg, 1928, p 66

13 Spanlang, H. Ztschr f Augenh **62** 21, 1927

14 Gilbert, W. Arch f Augenh **100-101** 329, 1929

15 Wright, R. E. Degeneration of the Cornea, Calcareous (?) and Fatty, Arch Ophth **15** 803 (May) 1936

The purpose of this article is to report a case of primary lipid dystrophy under observation at the present time. This dystrophy is associated with hypercholesteremia.

REPORT OF A CASE

History—G. C., a Negro farmer aged 61, was first seen in the medical clinic of Duke Hospital July 12, 1944, complaining of recurring temporal headaches of two years' duration and failing vision of three years' duration. The family history revealed hyperthyroidism in a sister and cardiovascular disease in the father. The past history disclosed that the patient had been struck on the left brow with an ax at the age of 6, without injury to the eye. Physical examination gave the following pertinent findings, oxycephaly, dirty, carious teeth, bilateral corneal opacities, lipoma of the scalp over the occiput, lipoma of the left axilla, and slight enlargement of the left ventricle. The blood pressure was 210 systolic and 115 diastolic. The patient was judged to have hypertensive cardiovascular disease with arteriosclerosis, lipomas and corneal opacities. He was then referred to the eye clinic for diagnosis and treatment of the ocular condition. In the eye clinic, the patient gave a history of "irritation" of the left eye for the previous four years. This consisted of an attack of injection of the conjunctiva, pain and lacrimation. The inflammation subsided without treatment. This was followed by similar attacks at about three month intervals in the left eye only. "Smoky" vision in the left eye was noted about two years prior to examination. Twelve months before, a similar attack occurred in the right eye, and this was followed shortly by a bilateral attack. At the time of examination the only complaint was diminishing vision in the left eye. The patient had never injured either eye and had had excellent vision until the onset of the present illness.

Examination—Adnexa were normal. There was moderate conjunctival injection of the right eye. A grayish opacity was present in the posterior layers of the right cornea in a small area just inside the limbus in the lateral aspect. The left eye was white and quiet. Two dense corneal opacities almost completely covered the left cornea from the inner and outer canthi, except for a small area above and below the pupillary area (fig 1). The opacity was so dense that the iris and pupil could be only vaguely seen and the pupillary reactions could not be determined. It was yellowish white and heavily vascularized from both the inner and the outer canthus. Both eyes stained with fluorescein, and a small spot of superficial ulceration was found at the limbus of the right eye inferiorly. The left eye did not take a stain. Examination of the right eye with the slit lamp revealed no aqueous flare or keratic precipitates. Corneal sensitivity was normal. Vision was 20/20 in the right eye and 20/400 in the left eye. Tension appeared normal to digital examination. The house officer's impression was that of corneal dystrophy of unknown cause, but probably of nutritional origin. Oral administration of vitamins was prescribed, as well as instillation of drops of cod-liver oil for the right eye. Instructions were given to return in three months.

Course and Examination—On October 24 the patient returned with no complaints. He had had no symptoms since he had been last seen. Vision was unchanged. Examination with the slit lamp showed no change except for increasing density of the opacities in the left eye. Both eyes were white and quiet. No stain was taken by either cornea. No keratic precipitates or flare was seen.

Feb 13, 1945. The only change noted in the examination was that the opacity in the left eye was much denser and had involved the entire cornea. Vision was 20/20 in the right eye and was limited to light projection in the left eye.

May 15 He returned with the complaint that he felt as though he had had something in his right eye for the past seven days and since then the eye had been painful and injected. He reported no visual change in the right eye. Examination showed that vision in the left eye was limited to light projection. The eye was quiet and white, with a dense corneal opacity. Vision in the right eye was 20/25. There were marked conjunctival injection temporally and a ragged-appearing conjunctival ulcer, 2 mm in diameter, which stained with fluorescein, just outside the limbus at 9 o'clock. There were multiple, superficial tiny areas of staining over the lower third of the cornea. The deep opacity was unchanged in appearance and size. There was no circumcorneal injection, keratic precipitates or aqueous flare.

May 19 The patient was admitted to the hospital, and the piled-up, ragged tissue was debrided from the ulcer, so that the cauterizing agent would come in



Fig 1—Two dense corneal opacities in the left eye

direct contact with the base of the lesion. It was then cauterized with 7 per cent iodine and covered with a conjunctival flap. The postoperative course was uneventful, and the patient was discharged from the hospital on the fifth postoperative day, at which time the flap was holding well and the area took no stain. Subsequent examinations at two week intervals showed the superficial keratitis to be gradually clearing up, until, on July 12, 1945, the right eye was completely quiet and no area of staining could be found in the cornea.

Aug 16, 1945 The patient returned, stating that a bug had flown into his right eye a few days ago and since then the eye had become inflamed and painful. Examination, surprisingly, revealed a macerated black bug in the lower conjunctival fornix. It was removed. Examination with the slit lamp showed a number of the tiny superficial areas of staining on the lower third of the cornea. The opacity had definitely progressed toward the pupillary area and had also involved more of the substantia propria near the limbus. A few tiny vessels could be made out entering it in the middle of the substantia propria. No keratic precipitates or aqueous flare was seen. There was moderate conjunctival injection.

For the first time a fatty degeneration of the cornea was considered. Instillations of 1 per cent atropine and an ointment containing vitamins A and D were prescribed, and he was told to apply hot compresses to the eye as often as possible. Admission to the hospital was suggested, but the patient wanted to harvest his tobacco crop before coming into the hospital.

August 23 One week later, the right eye appeared unchanged except for continued progress of the corneal opacity toward the center of the cornea. It was feared that the same process that had involved the left eye was endangering the right. Arrangements were made to admit the patient for biopsy of the corneal lesions, complete work-up of the case and possible corneal transplant in the left eye.

September 24 The patient was admitted to the hospital. The history and physical examination failed to reveal anything that had not been discovered in the clinics. Examination with the slit lamp at this time showed the following condition:

Right Eye The cornea showed slight mixed injection (fig 2A). The corneal epithelium appeared roughened and stained with fluorescein in numerous tiny places over the lower third of the cornea, forming minute dots and larger, confluent areas. No superficial infiltration was present. The lesion of interest was a smudge of whitish, greasy-appearing material, which extended along the posterior layers of the cornea from the temporal limbus in a crescent-shaped, diffuse opacity from 7 30 to 10 30 o'clock. It began immediately in front of Descemet's membrane and extended forward into the stroma to various depths but never more than through half its thickness. There were tiny, glittering particles in this area which were a dull gold. There was little vascularization, although a few small vessels extended into the stroma from the limbus in the central portion of the stroma. No keratic precipitates or aqueous flare was seen. The iris and the lens appeared normal.

Left Eye The eye was white and quiet (fig 2B). The cornea showed dystrophy, which may have been an advanced stage of the process which was beginning in the right eye. Almost all the normal cornea was replaced by a yellowish white opacity, leaving only a small ring of comparatively clear cornea adjacent to the limbus. The opacity was dense and seemed to comprise all the layers of the cornea. It appeared as though all the central portion of the cornea had been replaced by a nodular mass, elongated irregularly and impregnated with small flocculent, chalklike deposits at various depths of the stroma. At various places the surface glittered, but no definite crystals could be seen. The vascular supply was extensive. It was derived from two large vessels, one on the temporal and one on the nasal side. These two large vessels, were derived, in turn, from the conjunctival network. Many deeper vessels penetrated into the substantia propria at greater depths and anastomosed with these superficial vessels. The precipitated white matter appeared to follow, to some extent, these vascular channels. The periphery was not entirely free from opacity. In it were small, discrete opacities at various depths. The anterior chamber and the iris could not be made out because of the degree of opacity of the cornea. Ophthalmoscopic examination of the right fundus showed some arteriosclerotic changes in the vessels but no hemorrhages or exudate.

Laboratory Findings—The white cell count was 8,040. The hemoglobin measured 15.4 Gm per hundred cubic centimeters, or 100 per cent. The urine was normal. The blood chlorides measured 508 mg per hundred cubic centimeters, the total proteins, 7.7 Gm, the albumin, 3.3 Gm and the globulin, 4.4 Gm, per hundred cubic centimeters. The albumin globulin ratio was 0.75. The serum

cholesterol (see "Comment") was 390 mg per hundred cubic centimeters (normal, 250 mg per hundred cubic centimeters) on September 26, 300 mg per hundred cubic centimeters on October 10 and 250 mg per hundred cubic centimeters on



Fig 2—Appearance of (A) the right eye and (B) the left eye

October 25 The blood sugar measured 105 mg per hundred cubic centimeters on October 11 and 120 mg per hundred cubic centimeters on October 13

The results of the dextrose tolerance test were as follows. The fasting blood sugar was 90 mg per hundred cubic centimeters, at the end of one-half hour the blood sugar measured 131 mg, at one hour, 180 mg, at two hours, 125 mg, and at three hours, 90 mg, per hundred cubic centimeters.

The reaction to tuberculin was positive in a dilution of 1:10,000. The Wassermann reactions of the blood and spinal fluid were negative. The basal metabolic rate was -6 per cent.

The skull appeared oxycephalic in the roentgenogram. There was no evidence of Schuller-Christian disease, xanthomatosis or any other condition causing lesions of the skull. A roentgenogram of the chest showed that the lungs were clear. There were moderate widening of the aorta and enlargement of the left ventricle. Roentgenograms of the hands and feet were normal.

A medical consultant could find no evidence of Schuller-Christian disease or of any other xanthomatous condition. He did consider the possibility that the patient had incipient diabetes with a high renal threshold. Neurologic examination and studies of the nose and throat revealed nothing abnormal.

Course in Hospital—The patient was placed on a high vitamin diet and received 1 drop of penicillin (1:2,500) in the right eye every hour and 1 drop of 1 per cent atropine three times a day in the right eye. Compresses of warm boric acid solution were applied to the eye. Two superficial roentgen treatments of 100 r each were given to the right eye one week apart. A scraping from the right cornea made on July 1, 1945 revealed intracellular and extracellular globules of fat, after which a deeper specimen was taken from each cornea for biopsy. On October 13 he was placed on a low fat, low cholesterol diet. A corneal transplant, using a 4 mm trephine, was made on the left eye on October 16. The iris and lens appeared normal. The patient had an uneventful postoperative course, the sutures being removed on the third postoperative day, and he was out of bed on the tenth day. Five days prior to discharge he was given 20 mg of thyroid twice daily. Just before discharge the axillary lipoma was removed for examination. Examination with the slit lamp on his discharge, October 31, showed that the right cornea did not take a stain and that the deeper lesion was stable. The transplant was becoming vascularized and looked hazy. Vision was 20/20 in the right eye and was limited to counting fingers at 5 feet (150 cm) in the left eye. He was told to follow a low fat diet because of the high cholesterol content of the blood.

Pathologic reports on the various specimens submitted were as follows:

A superficial scraping was taken from the involved area of the right cornea, fixed in solution of formaldehyde and stained with sudan IV. Examination showed the presence of a great deal of fatty substance, the bulk of which was extracellular. However, there were many macrophages which contained fatty granules in their cytoplasm. A similar preparation made from a normal cornea failed to reveal any fatty substance. The epithelial cells could not be examined carefully with this stain for fat.

A similar biopsy specimen taken from the left eye and fixed in both Zenker's fluid and dilute solution of formaldehyde U. S. P. failed to stain with hematoxylin and eosin satisfactorily. This problem was also encountered by Berliner¹⁶ in the staining of a cornea removed at autopsy in a case of Hurler's syndrome (lipochondrodystrophy), in which there was a lipid degeneration of the cornea following

16 Berliner, M. L. Lipin Keratitis of Hurler's Syndrome. Clinical and Pathological Report, Arch. Ophth. 22:97 (July) 1939.

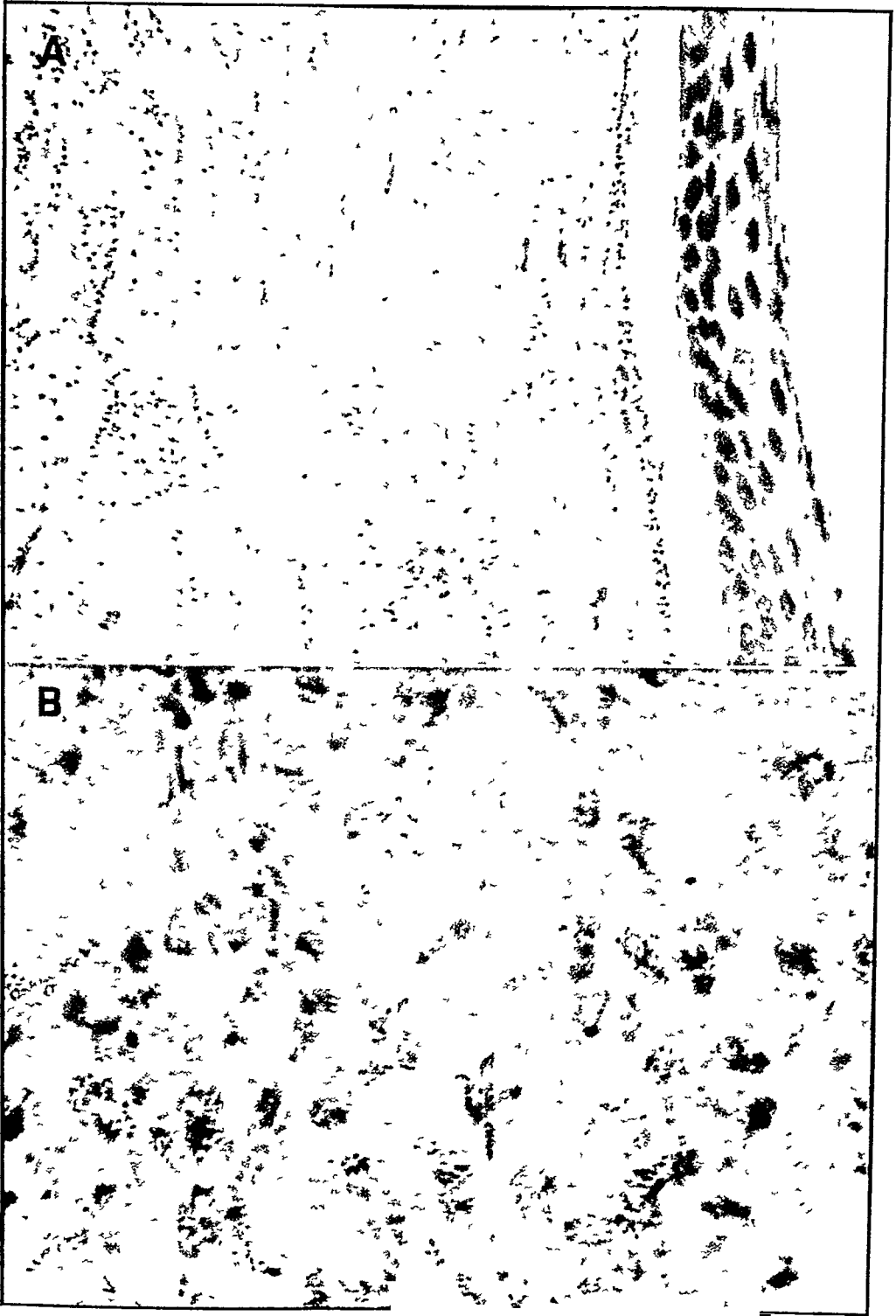


Fig 3—*A*, section through disk of cornea removed for corneal graft (hematoxylyn and eosin stain) *B*, section through corneal stroma stained with sudan IV showing numerous intracellular and extracellular fatty deposits

keratitis The tissue took a stain for fat (sudan IV) well, and no fat globules were seen, however, many needle-like crystals, 5 to 10 microns in length, took the stain for fat Polariscopic examination showed them to be doubly refractile cholesterol crystals These crystals lay either in the cytoplasm or between the epithelial cells Bowman's membrane could not be demonstrated in these sections

The disk of cornea removed in the transplantation operation was sectioned, and one-half was fixed in Zenker's fluid and the other in dilute solution of formaldehyde U S P Again, there was difficulty in securing a satisfactory stain with hematoxylin and eosin However, after several attempts, one was made in which the cellular detail could be clearly made out (fig 3) The stain for fat took well (fig 3 B) The corneal epithelium appeared normal Bowman's membrane was present in places and absent in others Where present, it appeared less refractile than normal Cellular infiltration and vascularization were present in the anterior two thirds of the stroma The deeper layers of the substantia propria were less heavily involved The endothelium and Descemet's membrane were not involved No fat globules were present in the epithelium Numerous capillaries, consisting of simple, endothelium-lined tubes, were seen coursing in various directions through the anterior two thirds of the stroma Prominent around these vessels, especially in the superficial layers, were focal accumulations of macrophages with rare lymphocytes These were absent in some areas The lamellae were thickened and not easily identified Large and small globules of fat were numerous both within the macrophages and, more often extracellularly These globules were most conspicuous in the deeper portion of the cornea, where the cellular infiltration was least conspicuous A few fibroblasts were seen in the superficial layers of the stroma No fatty acid crystals were noted, and polariscopic examination revealed no doubly refractile cholesterol crystals

Pathologic examination of the tumor removed from the left axilla¹ showed a typical lipoma

Further Course—On November 11, one week after discharge, the patient returned for an examination, at which time his condition was the same as on discharge On December 9 examination of the left eye with the slit lamp showed that the transplant was much more opaque, with several large vascular loops entering it in the middle of the stroma Most of the opacity was posterior Vision was limited to perception of moving fingers in this eye A tiny injected nodule was present under the conjunctiva, at the insertion of the lateral rectus muscle The patient was not seen again until Jan 11, 1946, at which time it was found that the nodule close to the insertion of the lateral rectus had increased greatly in size An unusual change had taken place in the peripheral zone of the cornea and about the transplant It was definitely clearing For the first time the iris and pupil could be clearly made out Examination with the slit lamp showed that the heavy, yellowish white opacity had been replaced, or absorbed, leaving many whitish, flocculent opacities at various depths The transplant was quite opaque A dense, yellowish white opacity was present over the posterior portion of the stroma of the transplant, and on it many discrete crystals sparkled under the light Vision was limited to perception of moving fingers

The patient was admitted for biopsy or excision of the subconjunctival nodule Except for the change in his left eye, physical examination showed that his condition was the same The cholesterol of the blood measured 227 mg per hundred cubic centimeters At operation, a firm mass, 10 by 5 by 3 mm, was observed to be securely attached to the sclera just beneath the lower portion of the tendon

of the lateral rectus (fig 4) It was immovable and rather vascular It could not be dissected free from the sclera, so, with a keratome, it was removed by sharp dissection flush with the sclera No foreign body was seen The lateral rectus was not involved in the mass The incision was closed with a running black surgical silk suture The postoperative course was uneventful, and the incision healed well The suture was removed on the sixth postoperative day

Ten weeks after operation the mass had not recurred The excised tissue was fixed in Zenker's fluid Histologic examination showed a nonspecific granu-



Fig 4—Granuloma in the sclera near insertion of the lateral rectus muscle

lomatous type of inflammatory process with many scattered giant cells Macrophages, plasma cells and a few lymphocytes were also present The arrangement was not in accordance to any particularly significant pattern, and no necrosis was present Stains for acid-fast organisms revealed no tubercle bacilli No foreign bodies were seen Stains for fat revealed small globules of fat in some of the macrophages but no foam cells typical of lipidosis It was impossible to determine the exact nature of the inflammatory reaction, but a foreign body reaction could not be ruled out The histologic picture was not suggestive of tuberculosis or lipidosis Material taken from the left conjunctival sac yielded no fungus on culture

COMMENT

Primary fatty dystrophy has been described as beginning either peripherally or centrally¹⁷ In the cases of peripheral origin the lesion usually starts as an opacity deep in the stroma close to the limbus The opacity gradually progresses centrally, although in some cases it has remained stationary while under observation, in still others exacerbations of activity have been associated with symptoms There is usually a relatively clear zone close to the limbus, although in the deep portions there may be some discrete opacities The opacity is always heavily vascularized, both by deep-looped vessels and by superficial, dilated and tortuous vessels derived from the conjunctiva

The central lesions tend to be small and localized, although they may involve the entire cornea except for a clear zone peripherally After observation of various stages of the condition in the present case, from appearance of the peripheral lesions through the development of the heavy central opacity to the definite clearing of the periphery, it seems plausible that the central lesions may have been a late stage of the peripheral lesion and that all fatty dystrophies follow the same pattern of progression

Primary fatty degeneration is almost invariably bilateral A grayish yellow opacity is first observed, which later becomes fibrosed, with yellow masses and whitish plaques visible, in most of the reported cases needle-like crystals being present The active lesions spread toward the center of the cornea and become more superficial Apparently, painful symptoms result when the epithelium is involved

The etiologic factors are obscure Endocrine disturbances, faulty fat metabolism, hypercholesteremia, circulating toxins, poor diet and repeated minimal trauma have been considered as causative factors

In 6 of the reported cases of lipid dystrophy blood cholesterol findings were listed In 3 of the cases values were within normal limits¹⁸ Two of them were within the upper limits of normal¹⁹ In the case reported by Meesmann¹² the blood cholesterol was 360 mg per hundred cubic centimeters In the case described here the blood cholesterol varied between 390 and 227 mg per hundred cubic centimeters (normal 250 mg per hundred cubic centimeters) When, after the second determination, the value was found to be 300 mg per hundred cubic centimeters, the patient was placed on a low fat, low cholesterol diet After this diet had been followed for twelve days the blood cholesterol was 250 mg per hundred cubic centimeters

17 Duke-Elder, W S Text-Book of Ophthalmology, St Louis, C V Mosby Company, 1938, vol 2, pp 2022-2024

18 Kamocki¹ Katz and Delaney²

19 Tertsch³ Bachstez⁴

The following biopsy observations were made repeatedly on corneal specimens in these cases

1 Fatty infiltration occurred throughout the layers of the cornea in varying degrees. The epithelium, Bowman's membrane, the substantia propria and the endothelium were involved, but this deposition of fat was mainly observed in the stroma

2 Lamellae of the stroma showed degenerative changes and vacuolation

3 There was infiltration with large mononuclear macrophages the cytoplasm of which was filled with fatty granules. Most of the fat was observed in these cells

4 Crystals became more prominent as the lesion became older, and as this process proceeded the macrophages became fewer

5 In most cases more fat was shown with a sudan stain than with an osmic acid stain. Thus, more cholesterol than neutral fat was present

An interesting problem in cases of this condition is to determine the presence or absence of any ocular inflammation which may be the cause of the lipid dystrophy. Assuredly, primary fatty dystrophy is rare.²⁰ Heath²¹ stated, however, that such an entity does not exist, but that "lipid keratitis," of unknown origin, is always associated with low grade uveitis

The patient whose case is described here has been followed for twenty-one months, with examinations at intervals of from one week to three months. At no time has any evidence of intraocular inflammation been noted in either eye. As a matter of fact, for over a year, the diagnosis of primary lipid dystrophy was not considered and evidence of inflammation, especially in the left eye, with the more advanced lesions, was sought. There were three periods during which superficial staining was found in the right eye. However, no symptoms were noticeable and the presence of intracellular and extracellular fat globules among the epithelial cells may account for the desquamation of the epithelium.

The nodule that arose from the episclera and sclera in the left eye presents an interesting pathologic problem. Sections cut through various portions of the mass revealed a nonspecific granulomatous type of inflammatory process. A foreign body reaction could not be ruled out. The fact that a black surgical silk traction suture was placed directly through the area from which the granuloma arose, during the corneal transplantation, may explain a foreign body reaction. However, no foreign body was seen at operation or in the specimen.

The reduction of the density of the opacity that occurred at the same time that the nodule developed may represent regular progression of the

20 Duke-Elder¹⁷ Shapira, T. M. *Am J Ophth* **16** 1080, 1943

21 Heath, P. *Lipid Interstitial Keratitis*, *Arch Ophth* **13** 614 (April) 1935

primary fatty dystrophy or may have resulted from the increased vascularity caused by the granuloma

SUMMARY

A case of primary lipid dystrophy with hypercholesteremia is presented. The patient has been followed for twenty-one months, and the lesion in the left eye has progressed steadily and asymptotically without evidence of inflammation on examination with the slit lamp.

A corneal transplantation was done on this eye, and pathologic studies of the transplant and of biopsy specimens of the cornea of both eyes revealed marked deposition of fatty globules in both corneas. Doubly refractile cholesterol crystals were seen in the epithelium of the left eye.

After corneal transplantation in the left eye, a granuloma developed in the sclera near the site of insertion of the lateral rectus muscle. It was removed, and pathologic study revealed a nonspecific granulomatous type of inflammatory reaction. This may have been a foreign body reaction, resulting from a suture placed through the site of origin during the operation.

The peripheral zone of the left cornea cleared up considerably at the same time that the nodule developed. It is suggested that this may be coincidental and that it represented the natural course of primary lipid dystrophy.

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ESOTROPIA FOLLOWING OCCLUSION

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IT IS commonly known that temporary loss of vision in one eye may precipitate heterotropia in an infant, but ophthalmologists prescribe monocular occlusion in older children and adults with little concern that persistent esotropia may result. For example, prolonged patching of the better eye is used in the treatment of unilateral amblyopia and prolonged monocular bandaging in the treatment of corneal inflammations. The fact that esotropia has received little attention as a complication of occlusion suggests that it is rare in older children and adults, however, a review of 1,000 cases of esotropia observed in the eye clinics of the State University of Iowa College of Medicine and the University of Oregon Medical School revealed 4 such cases. Medicolegal problems were involved in 3 of the 4 cases, therefore, these cases are reported as representative of a serious, but little known, complication of a standard therapeutic and diagnostic procedure. An analysis of these cases suggests means of preventing and treating the complication.

REPORT OF CASES

CASE 1—An 8 year old white boy complained of impaired vision in the right eye. Cycloplegic refraction revealed 3 D of hyperopia and 1 D of astigmatism in each eye. Visual acuity was 20/20 in the left eye, but the right eye could be corrected to only 20/100. There was no manifest deviation, but postcycloplegic examinations with the Maddox rod and cover tests revealed an esophoria of 6 prism diopters for distant and 9 prism diopters for near fixation. Prism convergence was 12 diopters and prism divergence 3 diopters. The vertical vergences were 2 prism diopters. Ductions were full, and binocular rotations were concomitant when measured with a red and green filter projection system of the type described by Lancaster¹. The full cycloplegic correction was prescribed. The parents were advised that occlusion of the left eye would be considered after the patient had worn this correction for six weeks, but a few days later the parents became impatient and covered the left lens. When the patch was removed six weeks later, visual acuity in the right eye was improved to 20/70, but the boy described double vision. A concomitant esotropia was present, varying from 7 to 10 degrees for distant fixation and up to 35 degrees for near fixation.

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This paper was read at the Ninety-Fifth Annual Session of the American Medical Association, Section on Ophthalmology, San Francisco, July 3, 1946

1 Lancaster, W B. Detecting, Measuring, Plotting, and Interpreting Ocular Deviations, Arch Ophth 22 867-880 (Nov) 1939

(33 cm) On the major amblyoscope the boy was able to fuse simple targets only when the instrument was adjusted exactly to the angle of the squint. Occlusion was discontinued, but spontaneous recovery did not occur in the ensuing week. Instead, the deviation increased several degrees. Orthoptic exercises were then started.² After a month of training with the major amblyoscope and the Remy separator, the boy was again able to maintain single binocular vision for distant fixation, but he was unable to fuse near objects, owing to overconvergence. A 4 mm recession of the medial rectus muscle of the right eye reduced the deviation to orthophoria. After operation the boy regained comfortable single binocular vision without further orthoptic exercises and remained asymptomatic during the year that he was observed.

In this case the parents assumed responsibility for occluding their child's eye, consequently, there was no medicolegal problem. In the second case, the referring ophthalmologist was responsible for the occlusion and was faced with a malpractice suit.

CASE 2—A 12 year old white girl had had periodic esotropia, corrected with glasses, at the age of 3 years. She was 11 years old when she first consulted the referring ophthalmologist with a complaint of reading discomfort. At that time corrected visual acuity was 20/100 in the right eye and 20/20 in the left eye. The cycloplegic refractive error was 4 D of hyperopia in each eye. There was no manifest deviation, but the cover and uncover tests revealed 5 to 7 prism diopters of esophoria for distant fixation. The ophthalmologist advised the parents that there was little hope for restoration of normal visual acuity in the amblyopic eye but stated that there was nothing to lose by occlusion of the better eye. The full cycloplegic correction was prescribed with an occluder over the left eye. When the patch was removed six weeks later, the child described diplopia, and the amblyopic eye was grossly convergent. During the ensuing two months the diplopia gradually disappeared, misleading the family into believing that spontaneous recovery was occurring. Then it became apparent that the deviation would be permanent, and a malpractice suit against the physician was filed. I examined the patient two weeks later.

The patient had a concomitant right esotropia of 15 degrees for distant and of 25 to 40 degrees for near fixation. With a red and green filter projection system, a 15 degree central scotoma could be plotted in the right eye with the left eye fixating.³ With the major amblyoscope adjusted to the angle of her deviation, the child could fuse simple two dimensional targets over a range of a few degrees. Occlusion of the better eye was resumed to break up suppression, and intensive orthoptic exercises were initiated to increase the amplitude of fusional movements. After two weeks of orthoptic treatment there was no change in the findings, therefore recession of the medial rectus muscle of the right eye was done. Orthoptic training was resumed on the first postoperative day and continued for two weeks before the patient was able to maintain comfortable single binocular vision. Two months after operation measurements with the Maddox rod showed esophoria of 2 prism diopters for distant fixation and 4 prism diopters for near fixation. Prism convergence was 18 diopters and

2 Swan, K C, and Laughlin, E. Binocular Orthoptic Training for Amblyopic Patients, *Arch Ophth* 32 302-303 (Oct) 1944

3 Swan, K C. Definition of Anomalous Retinal Correspondence, *Am J Ophth* 28 58-61 (Jan) 1945

prism divergence 4 diopters. The vertical vergences were $1\frac{1}{2}$ prism diopters. Visual acuity in the amblyopic eye had improved to 20/50. The child was able to bar read and had comfortable single binocular vision for the first time in several years. The favorable outcome of the case resulted in withdrawal of legal action against the referring physician.

Profiting by experience with these 2 cases, I have not prescribed prolonged occlusion in the treatment of patients with unilateral amblyopia with single binocular vision. Rather, lacquering of the spectacle lens is used to reduce visual acuity of the better eye to slightly less than that of the amblyopic eye.⁴ This procedure permits the patient to maintain peripheral fusion and thereby reduces the danger of converting an esophoria into an esotropia.

The third case differed from the previous two in that occlusion was prescribed for an inflammation of the lids, but an uncorrected refractive error was also an important factor.

CASE 3—Three months prior to admission, the patient, a 9 year old boy, had received a bee sting on the left upper lid. The eye was rapidly closed by swelling. A week later an abscess on the lid was drained by an ophthalmologist through a superficial incision in the skin. The eye was bandaged and compressed for another week. When the bandages were removed two weeks after the injury, the boy described double vision, and it was noted that his uninjured (right) eye was convergent. The family was advised that spontaneous recovery would occur. During the ensuing two months diplopia gradually disappeared, but the deviation seemed to increase. I then assumed treatment in the case, with the knowledge that a successful outcome was the only means of averting a suit against a fellow ophthalmologist, for the family considered their physician to have been negligent. Examination revealed visual acuity to be 20/30 in the right eye and 20/20 in the left eye. The ductions were full, and binocular rotations were concomitant. The cover test revealed 16 prism diopters of right esotropia for distant fixation and up to 60 prism diopters for near fixation. On the major amblyoscope, with simple disk targets adjusted to the angle of squint, the boy was able to fuse over a range of a few diopters. Cycloplegic refraction revealed 2 D of hyperopia in the left eye and 4 D in the right eye. A full correction was prescribed. With glasses, the deviation decreased to 8 prism diopters of convergence, and diplopia recurred. Two weeks of intensive orthoptic training greatly increased the boy's range of fusional movements, but he could not overcome the deviation. Therefore, a recession of the right medial rectus muscle was performed. On the first postoperative day the patient had single binocular vision with stereopsis. Two months later Maddox rod measurements showed orthophoria for distant fixation and 3 prism diopters of esophoria for near fixation. Prism convergence was 20 diopters and prism divergence 6 diopters. The boy was able to bar read. There was no change in the findings one year later. Suit against the referring physician was dropped.

CASE 4—A white man aged 27 was admitted with a complaint of double vision. He had worn glasses since childhood. Three years previously a cycloplegic refraction by an ophthalmologist had revealed $4\frac{1}{2}$ D of hyperopia. The full cor-

⁴ Pugh, M. A. *The Eye and Its Diseases*, Philadelphia, W. B. Saunders Company, 1936, p. 913.

rection had been prescribed because the patient had 8 prism diopters of esophoria for distant fixation and 10 prism diopters for near fixation. Prism divergence had been 3 D and prism convergence 25 D. Four weeks before admission the patient consulted a nonmedical refractionist for a routine examination of his eyes. He was advised that his glasses were too strong and that he had a "latent muscle imbalance." As a diagnostic procedure, monocular occlusion without correcting lenses was prescribed for a week. When the occluder was removed after eight days, the patient had diplopia. This was temporarily relieved by base-out prisms and a small hyperopic correction was prescribed by the refractionist. Then the patient noted a gradually increasing separation of the images. On his admission examination revealed uncorrected visual acuity to be 20/20 in each eye. With cover tests there was a concomitant alternating esotropia measuring 12 to 15 prism diopters for distant fixation and up to 35 prism diopters for near fixation. Single binocular vision could be produced with base-out prisms corresponding to the deviation. On the major amblyoscope the patient could fuse over a range of from 12 to 25 diopters of convergence. Cycloplegic refraction revealed $4\frac{1}{2}$ D of hyperopia. This correction was prescribed. A week later the patient's deviation had decreased several prism diopters, but he still had periodic diplopia. Daily training was initiated with the major amblyoscope and with the Remy separator. Prism divergence gradually increased up to 3 diopters, then the patient regained comfortable single binocular vision. A suit against the nonmedical refractionist was settled out of court.

COMMENT

It seems probable that prior to occlusion each patient maintained single binocular vision in spite of a strong convergent tendency. A slim reserve of fusional movements, maintained by daily use, was lost when binocular vision was disrupted for a time, however, at least two factors other than a diminished amplitude of fusional movements prevented spontaneous recovery. In the 3 cases in which measurements were obtained, the deviation became considerably greater after occlusion than was indicated by the previously made Maddox rod and cover tests, that is, the convergent tendency was increased by occlusion. It is known that the process involved in fusion exerts some restraint on any tendency of the eyes to deviate from the orthophoric position.⁵ This restraint is not completely removed when binocular vision is disrupted for a few minutes, as in the usual clinical tests, but may require several days of occlusion.⁶ In addition to diminished fusional movements and an increased deviation, loss of simultaneous binocular perception was another factor which prevented spontaneous recovery of single binocular vision in 2 of the cases. In these cases the response to a diplopia was suppression rather than an increased amplitude of fusional movements.

5 Bielschowsky, A. *Lectures on Motor Anomalies*, Hanover, N. H., Dartmouth College Publications, 1940, pp. 11-12.

6 Marlow, F. W. *The Influence of Prolonged Monocular Occlusion in Revealing Errors of the Muscle Balance*, *Brit. J. Ophth.* 4: 145-155 (April) 1920.

Considering these factors, it is evident that spontaneous recovery of single binocular vision is not to be expected in cases of esotropia developing after prolonged monocular occlusion and that prompt treatment would offer a favorable prognosis

SUMMARY AND CONCLUSIONS

Four cases of esotropia developing during periods of monocular occlusion are reported. Only limited conclusions can be drawn from 4 cases, but it seems that spontaneous recovery of single binocular vision is not to be expected from this uncommon, but serious, complication of a commonly used procedure. Treatment should be immediate, otherwise the deviation tends to increase and the amplitude of fusional movements to decrease, and suppression is likely to develop.

A latent convergent tendency seems to be the condition underlying development of esotropia from occlusion, therefore, in the presence of esophoria or uncorrected hyperopia prolonged monocular occlusion for diagnostic or therapeutic purposes should be used with caution. In the treatment of unilateral amblyopia in patients having single binocular vision, lacquering the spectacle lens to reduce visual acuity in the better eye is suggested as safer than total occlusion because binocular vision is maintained.

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ABSTRACT OF DISCUSSION

DR. PETER C. KRONFELD, Chicago. In the 4 cases on which Dr. Swan's paper is based, the patients were young hyperopic persons in whom occurred the striking phenomenon of moderate esophoria turning into pronounced esotropia during a period of monocular occlusion. That malpractice suits were filed in 3 of the 4 cases is indicative primarily of the gross change in the patient's appearance and visual comfort which were brought about by the occlusion, and only to a lesser degree of lack of good will on the part of the patient or his parents.

The phenomenon of esotropia following occlusion, as it occurred in Dr. Swan's 4 cases, can be broken down into two "subphenomena," namely, (1) impairment in the patient's ability to produce corrective fusional vergence impulses and (2) an increased, constant convergence impulse. The occurrence of the first subphenomenon after occlusion is thoroughly understandable and well known. The second subphenomenon is an interesting and new phenomenon. Observations in a large number of cases of esotropia and unilateral amblyopia, which is treated by occlusion of the better eye, do not indicate any consistent tendency toward an increased convergence impulse during the occlusion. Variations in the angle of squint occur in these cases, but they are not consistently in the direction of increased convergence. Thus, it would not be correct to say that monocular occlusion in cases of esotropia is conducive to an increase in the angle of squint.

In addition to the quantitative change, that is, the increase in the deviation as found by the cover test, a qualitative change occurred in Dr Swan's 4 cases. Originally the patients exhibited a noncharacteristic esophoria, whereas after the occlusion the neuromuscular condition was that of a convergence excess.

Proceeding from the simple and common to the complicated and unusual, Dr Swan's cases may be arranged in the sequence 4, 3, and 1 and 2, with the last 2 cases on the same level. The development of frank esotropia in case 4 is not surprising. A young person with esophoria and 4.5 D of hyperopia in each eye who has worn his spherical correction for a number of years and is suddenly deprived of it produces stronger accommodative impulses than normally. These are coupled with stronger convergence impulses. This overconvergence does not cause symptoms until the occluder is removed and the patient tries to resume the normal sensorial relationship of his eyes. Inefficiency of the mechanism of accommodation innervation under the unfamiliar conditions of seeing without glasses may account for the increase in the deviation. The patient's favorable response to proper glasses and orthoptic training is readily understandable. I cannot understand why the nonmedical refractionist instituted occlusion therapy in this case.

Case 3 is similar to case 4 except that glasses had never been worn. The patient had maintained binocular single vision by corrective fusional divergence impulses until the monocular occlusion necessitated by an inflammatory disease of the lids dealt a severe blow to the mechanism concerned with the corrective fusional movements. The fact that the patient was now forced to use exclusively, and without the aid of glasses, the eye with 4 D of hyperopia probably caused abnormal convergence impulses, resulting in a manifest and constant deviation. The occurrence of esotropia under such conditions is one of the many risks that are entailed in the practice of ophthalmology. I vaguely remember a reference to this situation in one of the older manuals on ocular therapeutics, the author recommending a routine phoria test before subjecting any eye to patching. Unfortunately, the state of inflammation and photophobia present in many of these situations makes phoria tests difficult and unreliable.

Cases 1 and 2 were characterized by the presence of unilateral amblyopia and parallelism under conditions of distance fixation. This parallelism was brought about and maintained by corrective vergence impulses originating from eccentric retinal areas. Such sensorial relationships between the two eyes are more easily disrupted than normal ones. The increased state of convergence can probably be explained again by the inefficiency and "awkwardness" of the amblyopic eye.

From the study of the paper, I got the impression that operation was resorted to in order to terminate an embarrassing situation. Theoretically, one would expect a favorable response of this form of esotropia to prolonged conservative treatment. It is remarkable that the recessions performed in 3 of the 4 cases corrected the convergence excess so beautifully and completely.

This is an interesting and stimulating paper.

DR GEORGE N. HOSFORD, San Francisco. We are indebted to Dr Swan for collecting, analyzing and bringing to our attention a group of cases which, fortunately, are not numerous, but certainly are troublesome.

At one time I used monocular occlusion extensively as a diagnostic procedure and in the treatment of amblyopia, and that I have no similar cases to report is due not to any precaution or forethought on my part but purely to good luck. Since I came under the influence of the teachings of the late Dr James White, I have used monocular occlusion but rarely for diagnosis and do not now believe that that procedure can tell the examiner anything about a patient which he cannot learn without it by other, more rapid and less troublesome, methods. Furthermore, in observing the results of ophthalmologists who do use and rely on it I have found that it is misleading, particularly in cases of double hyperphoria, unless one eye is occluded until it reaches a stable point, after which the patient must be left without occlusion and the eyes given time to return to the usual relationship of position. The other eye must then be occluded until the hyperphoria ceases to increase under the cover. Even with this tedious routine, the data obtained are difficult to interpret (if they mean anything at all), so no great harm will be done if the occlusion test is allowed to fall into disuse.

Corneal lesions present a different problem, as there is no adequate substitute for bandaging in cases of this type, but one must be on the lookout for the possibility of turning a phoria into a tropia. In the rare cases in which this possibility exists, perhaps the bandage could be left off for an hour or two daily. If one should have the misfortune to precipitate a tropia, one obviously should not temporize, but should at once institute adequate treatment, including surgical procedures if necessary.

DR JOSEPH PASCAL, New York. Dr Swan's paper brings up an extremely important point for the reason that it is the general impression in ophthalmology that monocular occlusion can do some good and never any harm. The fact that it may do harm is an important point to consider.

Without analyzing the cases, I think that these patients must have had poor or a subnormal fusion faculty. The use of lacquer in monocular occlusion, covering up the lens of the better eye, is excellent. But in cases in which monocular occlusion is used to develop function in the amblyopic eye, a combined procedure is more desirable—one by which the patient comes to the office for binocular fusional treatment, say every two days or every day, and at the same time is made to use the amblyopic eye monocularly over a period of time. I know that the main objection to prolonged ocular occlusion for diagnostic purposes, as Marlow suggested, has been that this procedure is hard on the patient, but the possibility of such an occurrence as the development of esotropia with diplopia or suppression has rarely been mentioned. The paper is a revelation to me and, I think, to many other men.

DR KENNETH C SWAN, Portland, Ore. Dr Kronfeld is correct about the reasons for suit. In 2 of the cases legal action was dropped when a successful outcome was assured.

One is impressed with the multiplicity of factors in every case of squint. There is no question that a disturbance of accommodative convergence mechanism was important in these cases, but one cannot be certain that it was the single predisposing factor.

It was striking that before occlusion there was little difference in the amount of latent deviation for distance and near fixation. After occlusion, there was excessive convergence with accommodation. This is an indication that the latter condition was of functional origin and therefore not a surgical problem. The deviation for distant fixation is corrected by operation, so that the patient is able to maintain single binocular vision and thereby exercise fusional movements by normal use. As amplitude is gained by normal use and orthoptic training, the functional over-convergence for near fixation decreases, and single binocular vision for near fixation is reestablished.

I have been unable to find references to squint following occlusion, but I agree with Dr. Kronfeld that cases must exist, for the literature contains warnings against the prolonged use of occlusion in the presence of esophoria.

Since the notice of this paper appeared, a few weeks ago, five ophthalmologists have advised me that they have observed similar cases in their private practice. I believe that the development of esotropia after occlusion is more common than the literature has led one to believe, for a physician is hesitant about reporting cases which may involve him in legal action.

PENTOTHAL SODIUM IN OPHTHALMIC SURGERY

GEORGE J THOMAS, M D

AND

MURRAY F McCASLIN, M D

PITTSBURGH

IN THE past decade intravenous anesthesia has shown a definite and consistent increase in its application and use. We feel that this form of anesthesia has a definite place in ophthalmic surgery for the following reasons:

- 1 The technic of administration is simple
- 2 The period of induction is short and pleasant
- 3 The usual psychic shock is absent
- 4 The depth of narcosis is controllable and sufficient for any ophthalmic procedure
- 5 The administration may be repeated without danger of becoming habit forming
- 6 The operative field is free of the anesthetist and his equipment
- 7 The intraocular tension is reduced 40 to 60 per cent

We do not advocate intravenous anesthesia for all types of ophthalmic patients. We wish to emphasize that the contraindications to the intravenous use of anesthetic agents must be observed. Children under 7 or 8 years of age, unless robust, are poor subjects. In addition to their natural fear and small veins, the inertia of the air and their narrow air passages hinder gaseous exchange and create an undesirable situation in view of their relatively high oxygen requirement. Such patients do very well under anesthesia induced with solution of tribromoethanol U S P and ether, since the former prevents psychic shock, which children frequently show during the induction period.

THE AGENT OF CHOICE

In a study of several anesthetics for intravenous use, we found pentothal sodium to have the following advantages over other agents. 1 It is equally, if not more, powerful and rapid in action. 2 Twitching is

Read at the meeting of the Pittsburgh Ophthalmological Society Nov 26, 1945

From the Department of Anesthesiology (Dr Thomas) and the Department of Ophthalmology (Dr McCaslin), University of Pittsburgh School of Medicine, the Eye, Ear, Nose and Throat Hospital and St Francis Hospital

1a1e 3 Postanesthetic nausea and vomiting are less frequent 4 Relaxation is more satisfactory 5 Recovery is more rapid

The data presented today are based on 3,050 administrations of pentothal sodium for all types of ophthalmic surgery The youngest patient was 7 years and the oldest 93 years of age

The amount of pentothal sodium used ranged from 3 to 45 grains (0.195 to 2.925 Gm) The duration of anesthesia extended from three to ninety-five minutes There were several patients who received repeated administrations within a short space of time, without ill effects We have administered pentothal sodium without serious results to several patients with coronary heart disease, several with bundle branch block and 2 with infarct in the ventricular septum

We are of the opinion that our good fortune may be attributed to the technic of administration and to the management of these patients during anesthesia and during recovery from the anesthetic

TECHNIC OF ADMINISTRATION

Administration of Pentothal—We shall not describe all the details of the administration of pentothal, since this is solely a problem for the anesthetist However, we wish to discuss in detail the preanesthetic preparation of the patient, some important steps in the administration of the anesthetic and the management of patients to be operated on for cataract We shall describe the procedure used for such an operation because this must be flawless, since a simple error may result in the loss of an eye This technic, however, is applicable to all types of ophthalmic operations

THE TECHNIC IN DETAIL

1 The patient should be in the hospital at least one day before operation

2 An enema should be given eight to twelve hours before operation

3. A hypnotic, preferably pentobarbital, should be given the night before operation, to determine the patient's idiosyncrasy to barbiturates and to provide a restful night

4 Sips of water are permitted until two hours before operation

5 A preoperative hypodermic, the usual dose of morphine and atropine sulfate, is sufficient, and proper preoperative medication is essential for smooth pentothal anesthesia Opiates are used The necessity for the use of atropine should be emphasized These preoperative agents control the parasympathetic hyperactivity and inhibit salivary and mucous secretions, thereby greatly reducing the incidence of complications such as coughing, sneezing and laryngospasm The preoperative medicament should be administered hypodermically forty-five minutes before injections of the anesthetic

6 Two drops of 4 per cent cocaine hydrochloride should be instilled in each eye thirty minutes before the scheduled time of operation. This will aid in preventing sneezing.

7 Instillations of cocaine should be continued in each eye every ten minutes before the patient goes to operation and repeated on his arrival in the operating room.

8 Instillations of cocaine are again repeated just before the preparation of the eye for operation.

9 In order to maintain a minimal dose of pentothal, we request the surgeon or the assistant to check over the instruments and prepare the sutures necessary for the operation before the anesthesia is started.

10 The venipuncture is made just as the patient is being prepared for the operation.

11 We have been using a 4 per cent solution of pentothal sodium for patients under 50 years of age and a 2 per cent solution for those who are 50 and older. One and one-half cubic centimeters of nikethamide is added to each gram of pentothal sodium for the latter group and for patients with a history of coronary disease or arteriosclerosis, in the belief that the nikethamide will dilate the coronary vessels, thereby increasing the oxygen supply and nourishment to the heart.

12 Pentothal is started in the usual manner and with the customary care. Three cubic centimeters of the solution is injected during a period of eight to ten seconds. Because relaxation comes on more slowly than unconsciousness, it is important that a pause of five seconds follow the injection of each 2 or 3 cc of the agent. An additional 2 or 3 cc is injected at the same rate as at the beginning, followed by another pause of five seconds. This procedure is continued until the desired plane of anesthesia is obtained.

13 To prevent or to correct mechanical obstruction we avoid using the oropharyngeal airway, for fear of causing laryngospasm. To prevent mechanical obstruction, we have used a tongue suture. If the tongue suture is inserted properly, there should be no bleeding, and the patient should have no discomfort when consciousness returns.

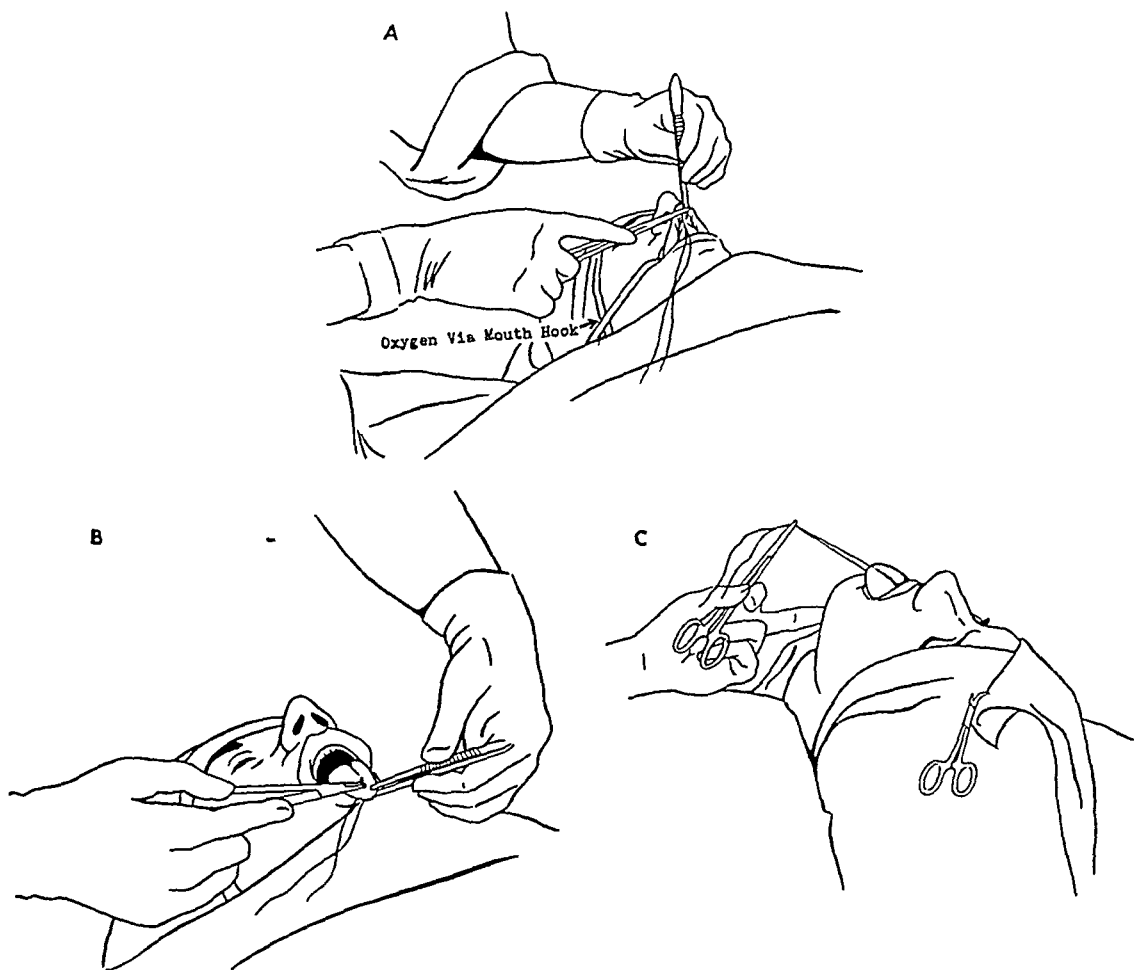
The technic of insertion of the tongue suture is as follows. The tongue is grasped with a thumb forceps and pulled forward and upward. The needle and the suture are inserted 1 fingerbreadth from the tip of the tongue, in the center and between the lingual vessels, as illustrated in *A* of the figure.

The second step is illustrated in *B*. The tongue is pulled forward and downward, and the needle and the suture are pulled through. The needle is removed from the suture.

The third step is illustrated in *C*. The ends of the suture are held with a forceps, and the mandible is supported in the manner illustrated.

It is important to support the mandible in order to obtain a patent airway. Furthermore, one must remember that too severe tugging on the tongue will result in great discomfort for forty-eight hours after operation.

14 Oxygen is administered through a mouth hook when the patient is in deep analgesia or in light anesthesia, as illustrated in *A* of the figure. Good color is of prime importance. A patent airway is of most importance.



Steps in insertion of the tongue suture. *A*, first step. The tongue is pulled forward and upward, and the needle and suture are inserted 1 fingerbreadth from the tip of the tongue, in the center and between the lingual vessels. *B*, second step. The tongue is pulled forward and downward, and the needle and suture are pulled through in the manner illustrated. *C*, third step. The suture is held with a forceps, and the mandible is supported in the manner illustrated.

15 The plane of anesthesia may be determined by the three reflexes (*a*) when the lid retractor is inserted (lid reflex), (*b*) when the superior rectus muscle suture retractor is inserted, and (*c*) when iridectomy is done. At this stage of the operation the patient should be in the proper plane of anesthesia for the section and the cataract extraction.

16 During the section and cataract extraction, slow injection of 0.5 cc of the pentothal solution is made, with a twenty second pause following each injection

17 One cubic centimeter of the pentothal solution is given when the cataract is delivered. The needle is removed from the vein when the dressings are applied to the eyes

18 The person who returns the patient to the room instructs the nurses to place a pillow under the head and shoulders, raise the back rest of the bed one notch, give oxygen with a mouth hook and make certain that the patient has a patent airway at all times

The O'Brien¹ block may be performed after preparing the eye for operation. We prefer this procedure because it adds another precaution in cataract surgery. This block prevents squeezing of the lids and consequent loss of vitreous should the patient be in too light a plane of anesthesia. The technic is as follows

A 1 inch (2.5 cm) needle, 25 gage, is inserted through the skin and tissues 1 fingerbreadth in front of the tragus of the ear and directed downward to the anterior part of the condyle of the mandible. One cubic centimeter of 2 per cent procaine hydrochloride is injected. The needle is slowly withdrawn and at the same time another cubic centimeter of the procaine is infiltrated into the tissues. With the thumb or index finger, pressure is applied over the infiltrated area. In two or three minutes the transitory paralysis of the orbicularis oculi muscle begins, this wears off in less than one hour

COMPLICATIONS AND THEIR MANAGEMENT

Complications with pentothal anesthesia are rare. However, some occur and should be managed without serious results. The most common is respiratory depression. The amplitude of the respiration, rather than the rate, is affected. We have found that oxygen administered through a mask, a catheter or a mouth hook is frequently sufficient to provide good color.

Other complications which may occur either in deep or in light anesthesia are coughing, laryngospasm and hiccup. These may cause alarming cyanosis and perhaps cardiac embarrassment if persistent. Such complications are undoubtedly due to parasympathetic hyperactivity. If they occur when the patient is under anesthesia, we aspirate the mucus or other material in the pharynx, deepen the anesthesia and immediately increase the flow of oxygen.

Trismus is another complication. This is undoubtedly a result of parasympathetic hyperactivity, which can be controlled with atropine

¹ O'Brien, C. S. Akinesis During Cataract Extraction, *Arch Ophth* 1 447-449 (April) 1929

Should this occur during anesthesia a nasopharyngeal tube should immediately be inserted and oxygen administered under pressure. Delay in this procedure may be serious.

POSTANESTHETIC COMPLICATIONS AND THEIR MANAGEMENT

The most common postanesthetic complication is respiratory depression. For this reason, all patients anesthetized with pentothal should have oxygen administered to them continuously after the operation until they have completely reacted. Furthermore, the entire nursing staff of all hospitals should be thoroughly trained in the proper management of patients receiving barbiturates. The nursing staff should be made to realize that the postoperative and postanesthetic care of patients is very important for uneventful recovery.

Postanesthetic opiates should be withheld, especially in the case of older persons, until the patient has completely reacted from the anesthetic.

If a patient has not reacted within two or three hours, it means that an overdose of pentothal has been administered. In this case treatment is as follows:

- 1 The patient is kept warm.
- 2 Oxygen is administered continuously.
- 3 The mucus is aspirated from the throat frequently.
- 4 Metrazol, 3 cc, is given intravenously. The injection is repeated in five minutes if necessary. (Incidentally, it has been found that metrazol is an efficient denarcotizing agent, as well as an excellent respiratory stimulant, if given in a sufficient dose.)
- 5 Hypertonic solution of sucrose is given intravenously for diuresis and dehydration of the brain and the lungs.
- 6 Repeated small transfusions of plasma are helpful.

CONTRAINDICATIONS

Pentothal sodium should not be employed or recommended when there is pronounced physiologic or mechanical interference with the respiratory function. It is contraindicated with inflammatory conditions of the neck complicated by edema of the glottis and with tumors of the neck encroaching on the glottis and interfering with respiration. Children under 7 or 8 years of age, unless robust, are poor subjects. It is inadvisable to use this agent with patients who have respiratory embarrassment due to cardiac decompensation. We feel that pentothal is contraindicated in the presence of bronchiectasis, severe anemia and shock.

CONCLUSIONS

A brief review of the technic of pentothal sodium anesthesia in ophthalmic surgery is presented, with special attention to the complications and their management, and to the contraindications. Pentothal is not a drug with which liberties may be taken. Special care should be exercised in maintaining an efficient airway at all times. A gas machine should always be on hand and ready for use should respiratory depression or other complications present themselves. Finally, the drug should be administered by a thoroughly trained anesthetist, who is competent to deal with any situation that may occur during the administration of this popular, but potent, agent.

Dr. John C. Dunbar photographed the various steps in the development of this technic.

4066 Penn Avenue

OPTOKINETIC AND OTHER FACTORS MODIFYING VESTIBULAR NYSTAGMUS

JOHN WOODWORTH HENDERSON, M D *

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IT HAS been common practice clinically to concentrate attention in ophthalmologic diagnosis on the two separate entities of "ocular" and "central" nystagmus. In so doing, optokinetic nystagmus has been relegated to a group of interesting phenomena which have little application in practice. The purpose of this paper is to present the accumulated knowledge regarding the modifying effect of optokinetic nystagmus and to add further experimental data.

Optokinetic nystagmus has been typified in ophthalmologic literature by the term "railroad nystagmus." When a subject allows his gaze to follow a moving object in the passing landscape, a slow deviation occurs which allows fixation to be maintained on the object. When an end position is reached beyond which head movement would be required for further fixation, a quick return to the primary position occurs, and the cycle is repeated as long as attention is maintained. The slow and quick components of the nystagmus thus are related to the direction of movement of passing objects and present the same relationship to each other as do the components of ocular motion produced by vestibular stimulation. Moving objects passing from left to right elicit a nystagmus identical with that observed by rotating a subject to the left, and vice versa.

Evidence of the close interrelationship of optokinetic and vestibular nystagmus has been steadily accumulating through the past several decades. Unfortunately, however, clinical practice and medical teaching have failed to keep pace adequately with the experimental findings. The usual concept which is presented to the student is that the nystagmus induced by rotation is purely a vestibular phenomenon. This is true only to the extent that angular acceleration (change in speed of turning) produces rotational response and angular deceleration elicits postrotational effects. Extensive modifications of response can be produced by many other factors, chief among which is the optokinetic nystagmus also produced by rotation.

* Walter R. Parker Scholar in Ophthalmology.

From the Departments of Ophthalmology and Anatomy, University of Michigan Medical School.

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Day		1				2				3				4				
Direction	Type *	To Right		To Left		To Right		To Left		To Right		To Left		To Right		To Left		
		Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	
Rab	bitRate																	
1	1/2	1	+	0	+	0	+	1?	+	0	+	1	+	0	+	0	+	0
	5	+	2	+	0	+	0	+	0	+	5	+	0	+	12	+	6	
	10	+	19	+	21	+	12	+	2	+	17	+	18	9T	10	7 1/2 T	14	
	1/4	1	+	0	+	0	+	0	+	0	+	4	+	0	+	0	+	1
	5	+	0	+	0	+	0	+	0	3T	13	3T	11	4T	5	+	6	
	10	8T	10	+	0	+	0	+	0	3T	11	4T	6	4T	10	2 1/2 T	5	
	20	6T	12	+	0	+	0	+	0	3T	10	4T	4	4T	7	3 1/2 T	6	
2	1/2	1	?	0	+	0	+	2	+	0	+	0	+	0	+	0	+	0
	5	0	2	SI	5	+	9	?	7	+	3	+	10	+	1	+	1	
	10	+	31	SI	18	+	17	?	15	+	25	+	17	+	0	+	6	
	1/4	1	+	0	+	0	+	0	0	+	0	+	2	+	0	+	0	
	5	+	0	+	5	SI	10	0	5	+	9	4T	5	+	3	+	5	
	10	8T	22	9T	7	+	9	0	5	6T	10	4T	6	5T	7	±	5	
	20	10T	19	10T	9	5T	11	3T	7	6T	11	4T	5	1T	9	0	6	
4	1/2	1	+	0	+	0	0	+	0	+	0	+	0	+	0	+	0	0
	5	+	8	+	3	Late	0	+	3	+	6	+	6	+	0	+	1	
	10	+	12	+	4	+	18	+	45	+	29	+	42	+	2	+	19	
	1/4	1	+	0	+	0	+	0	+	4	+	0	+	0	+	0	+	0
	5	+	2	+	0	+	16	+	14	+	8	+	9	+	0	+	4	
	10	+	0	+	0	5T	15	3T	17	8T	15	7T	7	+	5	4T	6	
	20	+	0	+	0	5T	13	3T	10	8T	13	8 9T	6	8T	15	5T	9	
5	1/2	1	+	0	+	1?	+	0	+	0	+	0	+	0	+	0	+	0
	5	+	3	+	3	+	7	+	3	+	4	+	2	+	0	+	2	
	10	+	11	+	5	+	57	+	30	+	16	+	7	+	5	+	5	
	1/4	1	+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	2
	5	+	5	+	0	+	8	+	0	+	2	+	0	+	7	+	0	
	10	+	7	+	0	9T±	15	+	0	+	7	+	0	0	7	+	1	
	20	9T	8	+	0	11T	8	+	0	12T	8	16T	9	1T	7	15T	7	
6	1/2	1	+	0	+	0	+	0	+	1	+	0	+	0	+	1	+	0
	5	+	4	+	3	0 → +	2	+	0	+	1	+	1?	+	0	+	0	
	10	+	6	+	2	+	1	+	6	+	0	+	6	+	0	+	1	
	1/4	1	+	0	+	0	+	0	+	0	+	0	+	0	+	1	+	0
	5	+	0	+	0	+	0	+	4	+	0	+	0	+	1	+	4	
	10	+	0	+	1?	+	0	+	5	+	0	6T	6	9T	3	4 1/2 T	7	
	20	+	0	+	0	+	0	4T	4	+	0	8T	7	6T	6	3T	6	
7	1/2	1	0	0	+	0	0	2	0	0	+	0	+	0	+	0	+	0
	5	SI	17	+	3	0	7	0	3	+	5	+	1	+	2	+	1	
	10	SI	23	+	11	0	18	+	Late	13	+	8	+	3	+	2	+	0
	1/4	1	0	0	+	0	0	2	0	0	+	0	+	0	+	0	+	1
	5	+	14	+	0	0?	9	Late	4	+	0	+	0	+	0	+	4	
	10	SI	12	+	0	+	7	7T	6	+	0	+	0	+	0	+	7	
	20	3T	11	12T	8	+	7	7T	6	+	10†	+	0	+	1	0	10	

* In this table, SI indicates slight nystagmus, Rot, rotational nystagmus, PR, postrotational nystagmus, +, nystagmus present throughout rotation, and T (with numeral), number of turns to which rotational nystagmus persisted

† Components reversed

‡ 1/2 means 1 turn per two seconds 1/4 means 1 turn per four seconds

Postrotational Nystagmus Induced in Rabbits

5				6				7				8 Not Blindfolded				Blindfolded	
To Right		To Left		To Right		To Left		To Right		To Left		To Right		To Left		Right	Left
Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	Rot	PR	PR	PR
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
-	0	+	0	+	0	+	0	+	14	+	7	+	0	+	0		
+	0	+	0	+	0	+	0	0	50	$+\rightarrow\pm$	29	+	0	+	0	11	11
-	0	+	0	+	0	+	0	+	1	+	4	+	0	+	0		
-	0	+	0	+	0	+	0	$+\text{SI}$	18	2T	12	+	0	+	0		
-	0	+	0	+	0	+	0	4T	19	2T	7	+	0	+	0		
+	0	+	0	+	0	+	0	3T	16	2T	11	+	0	+	0	5	5
+	0	+	0	+	0	+	1	+	1	+	0	+	0	+	0		
+	1	?	4	+	2	? SI	6	+	2	+	5	+	0	+	1		
+	11	+	10	+	7	SI	10	$+\rightarrow\pm$	10	6T	11	2T	6	2T	7	12	12
+	1	+	1	+	1	SI	2	+	1	+	3	+	0	+	0		
+	5	3T	4	+	4	SI \rightarrow 4T	3	2T	6	2T	4	4T	7	+	0		
3T	8	3T	4	6T	7	SI \rightarrow 3T	4	3T	8	2T	5	4½T	6	4T	5		
3T	7	3T	5	5T	6	SI \rightarrow 2T	3	3T	8	2T	6	4T	6	4T	5	9	7
+	0	+	0	+	0	+	0	+	1	+	1	+	0	+	0		
+	1	+	1	+	0	+	0	+	17	+	12	+	0	+	0		
+	5	+	1	+	20	+	13	7 T	62	6	32	+	0	+	6	17	22
+	1	+	0	+	2	+	0	+	11	+	6	+	0	+	0		
+	10	+	0	3T	14	+	0	3T	12	2T	13	+	0	+	0		
4T	15	+	0	3T	7	+	0	2T	17	1T	16	+	0	+	0		
4T	12	+	0	2T	16	16-18T	15	3	17	1T	13	+	0	7½T	4	9	7
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	1	+	0	+	0	+	0	+	0	+	0	+	0		
+	1	+	1	+	1	+	+	+	0	+	1	+	0	+	2	20	16
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	0	+	2	+	0	+	0	+	0	9T	0	+	0		
+	0	+	0	+	0	+	0	+	0	+	0	9T	0	+	0	9	10
+	1	+	0	+	1	+	0	+	2	+	0	+	1	+	0		
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0		
+	0	+	0	+	0	+	1	+	0	+	0	+	0	+	0		
+	0	+	0	+	0	16T	4	+	0	+	0	+	0	+	0	8	5
+	1	+	0	+	0	+	0	+	0	+	1	+	0	+	0		
+	1	+	1	+	2†	+	1	+	0	+	1	+	1	+	0		
+	12†	+	2	+	4†	+	1	$+\rightarrow\pm$	13	+	3	+	2	+	3	16	14
+	0	+	0	+	0	+	1†	+	4	+	0	+	0	+	0		
+	0	+	1	+	0	+	1†	1T	10	+	0	+	0	+	0		
+	13†	+	0	+	1†	+	1†	0?	8	+	0	+	0	+	0		
+	5†	+	1†	+	2†	+	0	0?	8	+	0	+	0	+	0	2+	8

Experiments had been performed by many workers demonstrating such modification, but it remained for Mowrer¹ adequately to analyze and correlate experimentally the interrelationship in the pigeon, and to some extent in man. He noted that the nystagmus present after rotation could be completely inhibited by the optokinetic nystagmus occurring during rotation and stated that this was due in part to a persistence of the optokinetic response which carried over into the postrotational period. This finding has been confirmed by my experiments.

Domestic white rabbits were utilized for our work, both because of their use in previously reported experiments and because of ease of procurement and handling. A series of 6 young males was subjected to repeated daily rotation in the horizontal plane with vision permitted during the tests. A hand-turned rotational table was used, with the animal's head fixed in a Czermak holder. Each animal was rotated through one, five and ten turns to the right, at a rate of one turn in two seconds, then through one, five, ten and twenty turns, at a rate of one turn in four seconds. This entire procedure was then repeated with rotation to the left. A rest period of approximately thirty seconds was allowed after each rotation. Postrotational nystagmus was recorded by visualizing the number of movements of the eyes occurring after deceleration. Rotational nystagmus was noted only as to its presence or absence.

The table presents the findings. If rotational nystagmus persisted throughout the period of rotation, it was designated by a plus sign (+). If it ceased during rotation, the number of turns through which it persisted was noted (e g, 3 T). Postrotational nystagmus was recorded numerically as the total of "beats" of nystagmus seen. At the end of eight consecutive days of rotation, the animals were blindfolded, and rotation was performed through ten turns at the faster rate and through twenty turns at the slower rate. This was done both to the left and to the right. The blindfold was quickly removed at the end of each rotation and the postrotational nystagmus observed. This is recorded in the last two columns of the table.

Certain facts become evident from examination of the recorded results. In all instances there was a definite reduction in the amount of postrotational nystagmus occurring when the animals were repeatedly rotated with vision permitted. The reduction was finally complete in the majority of instances, but it diminished at different rates in different subjects. In all cases postrotational nystagmus was present after blindfolded rotation of the animals at the end of the series of rotations. An example of these findings is presented graphically in chart 1. If rotational nystagmus was maintained throughout the period of turning, the postrotational response was consistently less. Toward the end of the series, if nystagmus was maintained in the animal throughout rotation,

1 Mowrer, O. H. (a) *The Modification of Vestibular Nystagmus by Means of Repeated Elicitation*, Comparative Psychology Monographs, Baltimore, Johns Hopkins Press, 1934, vol. 9, no. 5, (b) *Influence of Vision During Bodily Rotation upon the Duration of Post-Rotational Vestibular Nystagmus*, *Acta otolaryng* **25** 351-363, 1937.

the postrotational response was abolished, with few exceptions. If rotational nystagmus failed, the postrotational response was present to a greater extent and reached a level directly proportional to the number of turns through which the rotational response persisted.

After blindfolded rotation there was not a uniform correlation of response with the original postrotational nystagmus. However, those animals which had a relatively poorer postrotational nystagmus at the beginning had an even greater blindfolded response (animals 4, 5 and 6, table). It was noted also that in these subjects nystagmus was better maintained throughout rotation on the first day. However, those animals with a more marked postrotational response at the start of the series in general presented a blindfolded response which was less than

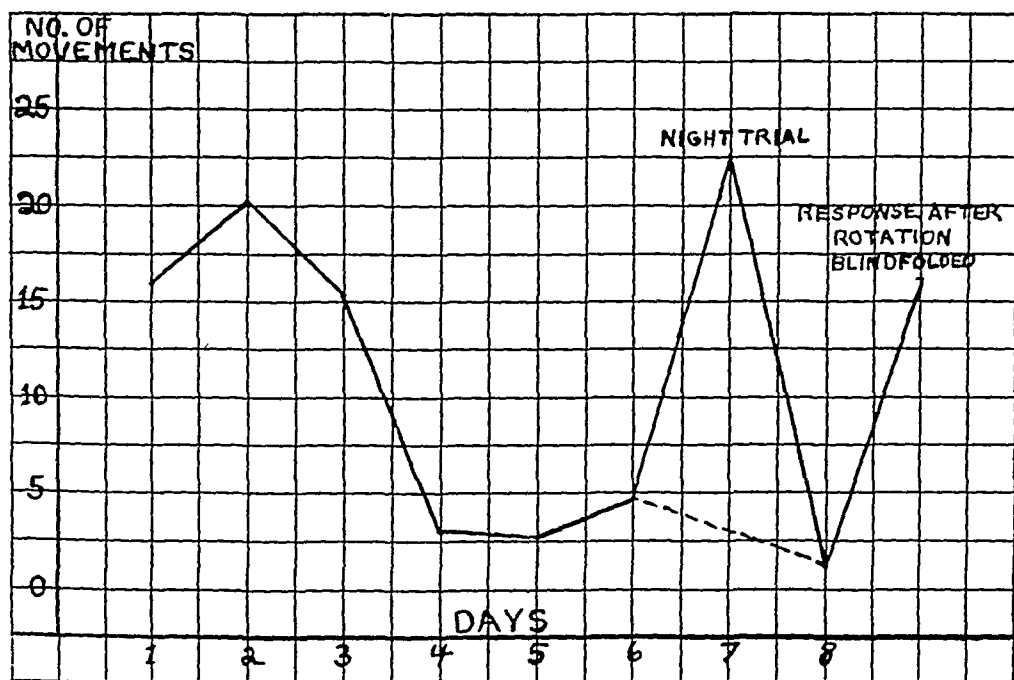


Chart 1—Average amount of postrotational nystagmus in all subjects after ten turns to the right in twenty seconds

that originally seen (animals 1, 2 and 7, table). Nystagmus was not maintained so well in the latter subjects throughout the rotation on the first day.

On the seventh consecutive day of rotation of the nonblindfolded animals, several of them demonstrated a greater amount of postrotational response than had been noted on previous days. This day's tests were performed late in the evening, after the rabbits had been in the dark for several hours, and all other tests were done in the afternoon. It was uniformly noted that those animals with greater responses were those which appeared more sleepy and less in contact with their environment. The following day all these subjects returned to their previous levels of reduction (chart 1, night trial). An example of the results with

rabbits 5 and 6, which failed to show an increase in response on the seventh day, is presented in chart 2. The latter subjects were wide awake and alert during the tests.

In 1 subject only (animal 7) an actual "reversal" of the expected postrotational response occurred. Here, the slow and quick components of the rotational nystagmus persisted after rotation, instead of showing a transposition of their components, such as was usually seen. These instances are marked by a dagger in the table.

Reduction of postrotational response has been variously interpreted by different workers. Hoshino² found a reduction on repeated rotation.

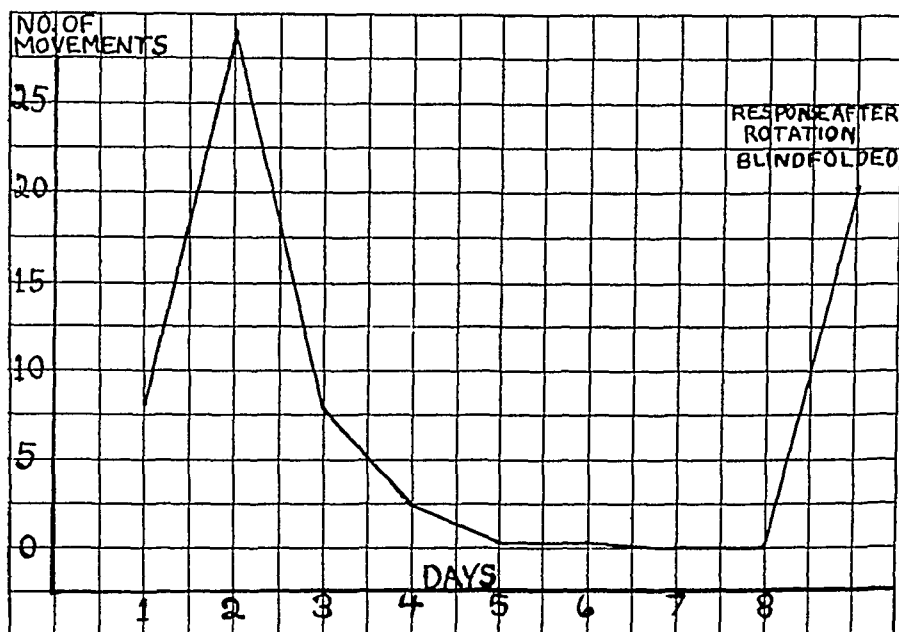


Chart 2—Average amount of postrotational nystagmus in rabbits 5 and 6 after ten turns to the right in twenty seconds.

in rabbits. Maxwell, Burke and Reston³ discovered a gradual decrease of postrotational response in rabbits on daily repeated rotation and claimed "habituation" of the animals to be the cause rather than vestibular damage. They also found an even more marked decrease when the animal's head was free rather than fixed. Pilz,⁴ continuing with the

2 Hoshino, T. Vestibulare Reflexbewegungen des Auges beim normalen Kaninchen, *Acta oto-laryng* 4 328-338, 1922.

3 Maxwell, S. S., Burke, V. L., and Reston, C. The Effect of Repeated Rotation on the Duration of After-Nystagmus in the Rabbit, *Am J Physiol* (March) 1924.

4 Pilz, G. F. On the Relation of After-Nystagmus to Rotation-Nystagmus, Direct Effects of Rotation, *Am J Physiol* 77 428-442 and 443-458 (July) 1926.

work reported by Maxwell,⁵ found that both the rotational and the postrotational nystagmus were reduced by repeated rotation. The postrotational response was decreased more readily, even to obliteration, although the rotational nystagmus was never completely lost. He also felt that retinal modification of labyrinthine effects occurred in the rabbit but that it was of low magnitude. Reports of reduction of postrotational nystagmus in man have been presented by several workers, namely, Griffith,⁶ Holsopple,⁷ Dunlap,⁸ and Dodge.⁹ The problem has been ably reviewed by Mowrer,¹⁰ and important contributions to the subject were made by him.

Mowrer used pigeons for his experimental work and investigated thoroughly the relationship of visual effects to vestibular responses. He concluded that three factors were operative in reducing postrotational nystagmus. He cited first the tendency on the part of the subject to fixate the visual environment after rotation. Second, in the pigeon, with the head free and with head nystagmus occurring, the continued reversal of vestibular stimulation produced by the head movement made the final deceleration stimulus at the end of rotation less effective in producing vestibular response. Third, he demonstrated a "post-stimulus persistence" of the visually induced rotational nystagmus which carried over after deceleration to inhibit further the postrotational vestibular response. Presumably, the first and third factors were active in reducing postrotational response in our series, but the second factor was eliminated because the rabbits' heads were fixed during the tests.

The influence of fixation on the results obtained may extend even further than by merely acting to inhibit postrotational response. If one considers that the initial rotational nystagmus is due to angular acceleration acting on the vestibular receptors, then this impulse should die

5 Maxwell, S. S. The Effect of Habituation on the Rotation-Nystagmus as Compared with the After-Nystagmus in the Rabbit, *Am J Physiol* **68** 125-126 (March) 1924.

6 Griffith, C. R. The Organic Effects of Repeated Bodily Rotation, *J Exper Psychol* **3** 15-46 (Feb.) 1920.

7 Holsopple, J. Q. Factors Affecting the Duration of Post-Rotation Nystagmus, *J Comp Psychol* **3** 283-304 (Aug.) 1923.

8 Dunlap, K. The Nystagmus Test and Practice, *J A M A* **73** 54-55 (July 5) 1919.

9 Dodge, R. Habituation to Rotation, *J Exper Psychol* **6** 1-35 (Feb.) 1923.

10 Mowrer, O. H. (a) The Influence of "Excitement" on the Duration of Post-Rotational Nystagmus, *Arch Otolaryng* **19** 46-54 (Jan.) 1934, (b) An Analysis of the Effects of Repeated Bodily Rotation, with Especial Reference to the Possible Impairment of Static Equilibrium, *Ann Otol, Rhin & Laryng* **43** 367-386 (June) 1934, (c) Some Neglected Factors Which Influence the Duration of Post-Rotational Nystagmus, *Acta oto-laryng* **22** 1-23, 1935, (d) footnote 1, (e) "Maturation" vs "Learning" in the Development of Vestibular and Optokinetic Nystagmus, *J Genet Psychol* **48** 383-404 (June) 1936.

out if the rotation were to be prolonged at the same rate. Actually, this appears to be the case in a number of the individual tests made in our series. In these tests rotational nystagmus continued up to a certain number of turns and then ceased. In some instances the same end point in number of turns was reached in successive rotations at similar rates of turning. In these cases there was uniformly more postrotational nystagmus, often of comparable amounts in successive tests. However, if fixation was maintained in the animal, producing an optokinetic type of nystagmus in an attempt to maintain orientation in space, the rotational response persisted throughout the period of turning. The animal then showed a corresponding reduction in postrotational nystagmus. It is probable, then, that both the attempts at fixation occurring during rotation and the fixation following deceleration are responsible for reduction in postrotational responses.

That the optokinetic nystagmus present during rotation can carry over as an inhibitory influence on response following deceleration has been substantiated further by the results with animal 7 in our series. Here, in several instances, the quick and slow components of the optokinetic response failed to reverse after deceleration. Instead of the expected postrotational vestibular response, the same ocular movements persisted which had been observed during rotation. In all the instances (indicated by dagger) in which this occurred (see table) the response during rotation was continuous. This appears, then, to demonstrate that an optokinetic impulse can carry over into the postrotational period and correlates with the results of Mowrer^{10c}. He found that pigeons which were rotated in the light and then placed in a darkened environment during the postrotational period showed this "inverse" postrotational effect. Attempts at fixation following rotation were eliminated by darkness, so the end effect must have been due to persistence of the optokinetic rotational stimulus.

Why such a response occurred in animal 7 of our series without the environment being darkened presents an interesting question. Mowrer's results in all his experiments with pigeons were surprisingly uniform. He also stated that the rabbit is not a suitable animal for such tests because of the variability of its responses. However, the basic structural differences between the avian and the mammalian brain may explain this apparent discrepancy. On the one hand, the pigeon, possessing a brain which has greatly enlarged basal ganglions and a relatively small amount of primitive cortex, has responses which are stereotyped. The mammalian subject, on the other hand, with the addition of a cerebral cortex, should present a variable response, conditioned by the level of cortical activity at the time of the experiment. Therefore variability should be the expected result, rather than stereotyped uniform response. This factor was well demonstrated by the

results gained on the seventh consecutive day of rotation. Here the animals, which were apparently lacking in attention because of the late evening hour during which the tests were performed, demonstrated a much greater postrotational response, and in 2 cases this was even greater than that seen at the start of the series. This would seem to indicate that a certain measure of cortical modification of the responses existed from the beginning and would also explain the individual variations between our animals recorded for the first day. It is obvious that there is danger in applying, unmodified, the results gained from experimentation on avian subjects to an analysis of the conclusions derived from experiments on man, since in the human brain the peak of cortical activity is reached.

The neuroanatomic background of the effects observed is not entirely clear. Mowrer¹¹ expressed the belief that the symptoms of nausea, vertigo, falling and past pointing seen with vestibular stimulation are likely due to stimuli resulting from the ocular motion produced by such vestibular activity. The point of origin of both the quick and the slow component of vestibular nystagmus has been shown to lie in the brain stem, the slow deviation being a direct result of action of the vestibular stimulus through the vestibular nuclei, and the quick return arising from the adjoining reticular substance (Lorente de Nó¹¹). That the quick component of vestibular nystagmus is not cortical has been shown by Ivy¹². Vestibular nystagmus, therefore, is thought to be a purely subcortical reflex phenomenon. Whether there is a cyclic repetition of stimuli in the vestibular nuclei occurring with the slow component, which then discharges the reticular impulse to produce the quick component, or whether the reticular substance discharges because of stimuli reaching it from a collicular level is not known. Ivy¹³ expressed the opinion that the quick component of vestibular nystagmus was not produced by a cerebral reflex arc but was probably due to a reflex by way of the muscle centers of the eyes, which was excited by stimulation of the kinesthetic sensory nerve endings in the extraocular muscles.

In contrast to vestibular nystagmus, optokinetic nystagmus may follow cortical pathways, since the element of fixation is involved. The visual impulses which reach the calcarine fissure reflexly act through areas 18 and 19 of Brodmann, the visual psychic cortex, by way of the internal corticotectal tract to the nuclei of the cranial nerves which govern

11 Lorente de No, R. Researches on Labyrinth Reflexes, *Tr. Am. Otol. Soc.* **22** 287-303, 1932.

12 Ivy, A. C. Comparative Study of the Relation of the Cerebral Cortex to Vestibular Nystagmus, *J. Comp. Neurol.* **31** 1-16 (Oct.) 1919.

13 Ivy, A. C. Physiology of Vestibular Nystagmus, *Arch. Otolaryng.* **9** 123-134 (Feb.) 1929.

movements of the eyes. Thus, fixation is maintained on the object, and a slow deviation results. Where the quick component of optokinetic nystagmus arises has not been demonstrated anatomically.

It is known that the quick return occurs in man when the deviation reaches a point beyond which head movement must occur in order to continue fixation. It is difficult to believe that the quick return can occur without the presence of proprioceptive stimuli from the extraocular muscles, although some investigators deny their existence. Adler¹⁴ stated that "there is certainly no anatomic or physiologic proof that proprioceptive sensation is mediated from the ocular muscles." On the other hand, specialized sensory endings about the extraocular muscle fibers have been demonstrated by several workers. Maximow and Bloom¹⁵ presented an illustration of such terminations. Hines¹⁶ described specialized endings in the extraocular muscle fibers in the rabbit which were distinct from the motor end plates and which degenerated when the oculomotor nerve was sectioned at the base of the brain. Her work is well documented with photomicrographs. Woollard¹⁷ observed similar endings in ocular muscle fibers and expressed the belief that his investigation suggested the origin of such nerve fibers to be in the mesencephalic nucleus of the trigeminal nerve, since degeneration was seen in this nucleus after section of the oculomotor nerve on the same side. The work of neuroanatomists on this problem has been well summarized by Ariens Kappers, Huber and Crosby,¹⁸ showing that the mesencephalic root of the trigeminal nerve may well be the site of cell bodies for such nerve endings. Corbin¹⁹ suggested that the sensory fibers to the extrinsic ocular muscles may be largely unmyelinated and may arise from the small cell component of the mesencephalic nucleus at the level of the oculomotor nucleus, since he could not trace such fibers in Marchi preparations. Although no secondary pathway to the somesthetic cortex from these receptors is known, it still is evident that there is consciousness of the position of the eyes with the lids closed.

14 Adler, F. H. Pathologic Physiology of Convergent Strabismus. Motor Aspects of Nonaccommodational Type, *Arch Ophth* **33** 362-377 (May) 1945.

15 Maximow, A. A., and Bloom, W. A Textbook of Histology, ed 4, Philadelphia, W. B. Saunders Company, 1942, fig 174.

16 Hines, M. Studies on the Innervation of Skeletal Muscle. III. Innervation of the Extrinsic Eye Muscles of the Rabbit, *Am J Anat* **47** 1-53 (Jan) 1931.

17 Woollard, H. H. The Innervation of the Ocular Muscles, *J Anat* **65** 215-223, 1931.

18 Ariens Kappers, C. U., Huber, G. C., and Crosby, E. C. The Comparative Anatomy of the Nervous System of Vertebrates, Including Man, New York, The Macmillan Company, 1936.

19 Corbin, K. B. Observations on the Peripheral Distribution of Fibers Arising in the Mesencephalic Nucleus of the Fifth Cranial Nerve, *J Comp Neurol* **73** 153-177 (Aug) 1940.

If such an impulse reaches the higher centers, then the quick component may be produced by cortical motor centers

The location of the mesencephalic nucleus is such that it might be possible for direct connections to exist in the midbrain between its fibers and the neurons constituting the nuclei of the extraocular muscles. In this way, the quick return movement may be produced. There is no work confirming or disproving this point, although cells of the mesencephalic nucleus lie in the midbrain, some of them very close to the oculomotor nucleus, or rarely in it. Others lie in the anterior medullary velum, close to the emerging roots of the trochlear nerve¹⁸

Another possibility is that the reticular centers of the brain stem play a role in the mechanism underlying the quick component of optokinetic nystagmus similar to that which they play in producing the quick component of vestibular nystagmus. The superior colliculus and the underlying regions, or tegmentum of the midbrain, are known to give rise to fibers which pass downward to the reticular formation of the brain stem. Thus the discharge, whether it arises from cortex or from proprioceptive connections direct to the motor centers of the extraocular muscles, could be sent by way of tectoreticular pathways to the reticular substance at the level of the vestibular nuclei, producing the quick return. This raises the question whether the quick component of the vestibular nystagmus might not also be mediated by such connections.

In the phylogenetic development of extraocular reflex connections, it is known that submammalian forms, either lacking a cortex or having a less differentiated cortex than mammals, have a definite pattern of optic nerve fiber endings which is laid down on the superior colliculus. In these forms optokinetic nystagmus is probably subcortical in nature. As the cortex develops and a secondary connection of the optic nerve fibers into the calcarine region by way of the lateral geniculate nucleus appears, there are progressively fewer fibers which reach the superior colliculus. Optic nerve fibers are still present in mammals, including some primates, they turn off to the superior colliculus without terminating in the lateral geniculate nucleus. Such a pathway to the colliculus has been noted in rabbits' and monkeys (Brouwer²⁰). These connections are to be differentiated from the pupillomotor fibers of the optic nerve, which turn off to the pretectal nucleus before reaching the lateral geniculate nucleus. It is evident, then, that there is a gradual shift in the proportion of afferent ocular connections from collicular to cortical levels, with a corresponding development of the colliculus into an important discharge path from the visual psychic areas of the cortex.

²⁰ Brouwer, B. *Anatomical, Phylogenetical and Clinical Studies on the Central Nervous System* (Herter Lecture for 1926), Baltimore, Williams & Wilkins Company, 1927.

It seems altogether probable that with the anatomic shift there is a corresponding functional shift of optokinetic functions from the superior colliculus to the cortex

There is, however, the possibility that some subcortical reflex responses are present in higher forms in reaction to visual stimuli, and that optokinetic nystagmus, for example, could still occur in the absence of the calcarine area. Scala and Spiegel²¹ presented work done on the dog and the cat which suggests that optokinetic nystagmus can be subcortical. In carnivores it is generally recognized that there are relatively more of the optic nerve fibers given off to the superior colliculus than in primates. These authors also showed that lesions of the superior colliculus interfered with the "subcortical" optokinetic nystagmus, although they made no statement as to relative change of quick and slow components. It is true, moreover, that such lesions made in the superior colliculus region might well interfere with the corticotectal pathways reaching the extraocular muscles via the superior colliculus from the visual psychic cortex.

Whether such a finding would hold true for primates remains to be demonstrated. It is possible that the higher the form, the more the optokinetic nystagmus is cortical in nature and the less the effect of subcortical connections. This would correlate with observations relating to the "power of attention" of the subject in modifying vestibular effects through cortical activity.

Regardless of the final outcome of work in determining which connections are actually involved, it seems possible that proprioceptive impulses may govern the quick component of nystagmus, both vestibular and optokinetic. This problem requires further study, and future investigations are planned in an attempt to determine such a relationship.

A further comment on the variability of response noted by different workers seems to be indicated. As was stated earlier in this paper, it is probable that cortical factors play a large part in modification of response. Mowrer^{1b} used the pigeon as an experimental subject, deriving stereotyped responses, which might be expected from an avian type of brain. The same author^{1a} stated

a variety of factors—presence or absence of vision, direction of rotation, emotional disturbance, relative duration of the successive rotation and rest intervals, fixation or non-fixation of the head, age and type of subject, etc—may be influential in determining the rate and extent of nystagmus reduction produced by any given schedule of repeated bodily rotation.

Hoshino² noted a variability in responses of the rabbit on successive days. Ivy¹² reported a considerable variation in the individual rabbit

21 Scala, N. P., and Spiegel, E. A. Mechanism of Optokinetic Nystagmus, *Arch Ophth* **21** 555-557 (March) 1939.

with the same stimulus and found that struggling inhibited the duration and number of movements of the "after-nystagmus" Mowrer¹⁰¹ presented evidence which "suggests that the duration of nystagmus is conditioned by a 'central' mechanism" He noted, further, that variations which are not vestibular could be explained by assuming that such a "central" mechanism might be modified by "characteristic differences in nervous disposition as well as by temporarily prevailing neural conditions" These factors appear to explain the variability of response recorded for our series of animals and confirm the observation that variability may well be expected in species in which cortical factors modify the lower reflex responses

SUMMARY AND CONCLUSIONS

Vestibular postrotational nystagmus is capable of modification by optokinetic nystagmus In most cases of our series postrotational response was abolished by repeated daily rotation This suggests that cortical influences are dominant over those of the vestibular level

There appears to be a poststimulus persistence of optokinetic rotational nystagmus which is effective in reducing postrotational response Our findings tend to support those of Mowrer in this respect

Variability of response has been shown to be the expected finding in the higher forms which possess a well differentiated cerebral cortex This tends to render less valid work which has been done using lower species whose response is mainly reflex in type This also supports the accumulating mass of evidence which invalidates the Bárány test as a precise diagnostic aid

The neuroanatomic background of optokinetic nystagmus is discussed and further lines of research are suggested

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CHANGES IN RETINAL ARTERIOLES ASSOCIATED WITH THE HYPERTENSIONS OF PREGNANCY

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DURING the past fourteen years I have studied the eyegrounds of approximately 2,500 women suffering from hypertension during pregnancy. In two previous reports¹ the observations made on some of these patients were analyzed and an attempt was made to correlate the changes in the eyegrounds with the degree of toxemia. It was found that the frequency and degree of such changes more closely followed the severity of hypertension, and consequently the toxemia, than any other single laboratory or clinical sign. The one outstanding and consistently reliable change observed in the eyegrounds was the degree of general and localized spastic constriction of the retinal arterioles.

ANATOMY OF THE RETINAL ARTERIOLES

Knowledge of the structure of the walls of the retinal arterioles helps one to understand better the local manifestations of angiospasm. The central artery in the optic nerve has the same histologic characteristics in microscopic sections as arteries of similar size in other parts of the body. Its muscular coat has a thickness of about one-eighth the diameter of the lumen of the artery. But, as Friedenwald² stated

On passing through the cribriform lamina the artery is very markedly altered. The internal elastic lamella becomes reduced to a single thin layer and disappears entirely after the first or second bifurcation. The muscular coat becomes reduced to a single layer of muscular fibers, and after one or two bifurcations the fibers no longer form a continuous layer but are separated from one another by small gaps. Since, by definition, arteries which do not possess an internal elastic lamella nor a continuous muscular coat are classified as arterioles, the whole retinal arterial tree except for those branches in or close to the optic disc is arteriolar.

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This paper was accepted as the candidate's thesis in partial fulfillment of the requirements for membership in the American Ophthalmological Society by the Committee on Theses.

1 Hallum, A V (a) Eye Changes in Hypertensive Toxemia of Pregnancy Study of Three Hundred Cases, *J A M A* **106** 1649 (May 9) 1936, (b) Eye Changes in Management of Hypertensive Toxemia of Pregnancy Five Year Study, *South M J* **31** 64 (Jan) 1938.

2 Friedenwald, J S, in Ridley, F, and Sorsby, A. *Modern Trends in Ophthalmology*, New York, Paul B Hoeber, Inc, 1940, p 77.

ESSENTIALS OF OBSTETRIC OPHTHALMOSCOPY

The present discussion is intended primarily for the obstetrician, appealing to him to do his own ophthalmoscopy. Of course, the best time to learn to use the ophthalmoscope is during the internship, when one is younger and more adept at learning new procedures. However, the obstetrician who had no training in the use of the ophthalmoscope during his hospital days can within a few weeks acquire the ability to gain invaluable information from the eyegrounds of almost every patient exhibiting hypertension during pregnancy. During the course of severe and moderately severe toxemia of pregnancy the most information is gained from the eyegrounds by making repeated examinations daily or every few days. A consultant ophthalmologist will be called in only once, or not at all, and if the obstetrician cannot do his own ophthalmoscopy the patient is the loser. Occasionally, she pays with her life or with the life of her baby when the obstetrician does not recognize the progress and severity of the toxemia and fails to terminate pregnancy. The eyegrounds are probably the best single indicator of the progress and severity of the toxemia.

In the early stages of learning the use of the ophthalmoscope, some help in the fundamentals from one's fellow ophthalmologist will be of great value. A good ophthalmoscope is essential, preferably one with the May head, and the illumination must always be bright. The most satisfactory ophthalmoscope and source of light is the giant electric ophthalmoscope, which operates off the house current, and the same small portable transformer is used as that which operates the usual office cautery.

Another essential requirement for good ophthalmoscopy is the dilation of the pupils. With instillation of 1 drop of a weak mydriatic, such as paredrine hydrobromide ophthalmic,³ the pupils will be semidilated in twenty or thirty minutes. They will remain semidilated for an hour or two, but accommodation is only slightly impaired. The examination of the fundi can be much more efficiently done in a semidark or dark room. If the patient is to go out into bright sunshine after this examination, it might be preferable to hasten the contraction of the pupils by instilling into each eye 1 drop of a weak miotic, such as 0.1 per cent physostigmine salicylate or 0.5 per cent pilocarpine nitrate. However, the patient should be warned that in a few minutes she will probably experience twitching of her lids, and possibly a drawing sensation in her eyes. This ciliary spasm lasts only a few minutes but often produces much more discomfort than does the small amount of photophobia, and for that reason the miotic had probably best be omitted.

3 Paredrine hydrobromide ophthalmic is a 1 per cent solution of *p*-hydroxy- α -methylphenylethylamine hydrobromide in distilled water, made tear isotonic with 2 per cent boric acid and preserved with merthiolate, 1:50,000.

The possibility of acute glaucoma being produced by the dilation of the pupils is remote, since glaucoma is rare in women of the child-bearing age. However, if acute glaucoma should be precipitated, the patient will complain of more or less severe pain in or about the eyes, and her vision will be noticeably impaired by the haziness of the corneas. The eyeballs will feel hard when palpated through the upper lids, and the pupils will be dilated. If acute glaucoma should be suspected, a miotic should be instilled into each eye six times at intervals of fifteen minutes, and the patient referred to an ophthalmologist. I have seen acute glaucoma develop in only 1 patient after this routine mydriasis and it was considered that she was fortunate in having her glaucoma discovered before it produced loss of vision.

SPASMS OF RETINAL ARTERIOLES

The first change observed in the normal retinal arterioles during a true toxemia of pregnancy is constriction of the lumen. In some patients this constriction may be localized to a single point, resembling a sausage-link constriction, as though a single fine silk thread partially constricted the arteriole. There can be a series of these localized constrictions, some elongated and spindle shaped and usually limited to the first half of the retinal arteriole. This is the portion of the arteriole nearest the optic disk, and the constrictions are seen more frequently in the nasal branches. These elongated, spindle-shaped constrictions appear as uniformly symmetric indentations of both sides of the arteriole and resemble the constriction that would be produced by stretching a glass tube, the middle section of which had been heated almost to the melting point. In searching for these localized constrictions, the examiner must adjust the ophthalmoscope to its very best focus, and if while looking at a section of an arteriole he slowly rotates the ophthalmoscope to and fro he will often bring the outline of the constrictions into better view.

In other patients the first change observed may be a generalized arteriolar constriction, so that, instead of the diameter ratio of vein to arteriole being the normal 3:2, the arterioles may be constricted so that the ratio is 2:1. As the severity of the toxemia progresses, the arterioles are usually seen to become more constricted, until the ratio increases to 3:1 or more. Usually the patients showing generalized arteriolar constriction also exhibit varying degrees of localized constriction. When there is a generalized arteriolar constriction beyond the ratio of 2:1, it is increasingly difficult to recognize localized variations in the diameter of the lumen. The addition of a localized spastic condition indicates an active progressive toxemia.

In estimating the vein-arteriole ratio, the examiner must be sure that he is comparing the diameter of a principal vein and its corresponding arteriole. The best place to make this determination is about

1 disk diameter from the margin of the disk, using either the superior or the inferior temporal vessels and being sure that neither the vein nor the arteriole has divided before reaching that point. If either the vein or the arteriole has divided before reaching the point of comparison, a wrong ratio will be obtained.

The arteriolar constrictions are proved to be spastic in nature when the degree and location can be seen to vary at subsequent examinations. Many patients were examined a few days after delivery, when the blood pressure had returned to normal and the formerly constricted arterioles had resumed their normal caliber and normal ratio. These constricted arterioles did not show compression of the veins at the

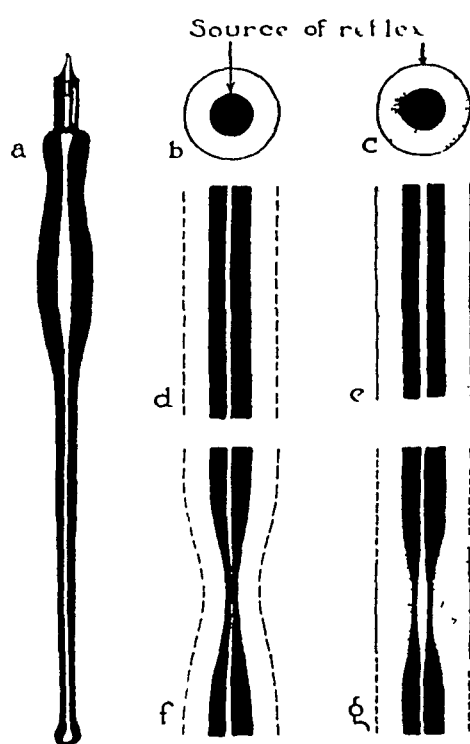


Fig. 1 (from Gans⁴)—Variations in the light reflex (see text for details)

arteriovenous crossing, nor did they show increased light reflex stripe. In fact, when there is noticeable angiospasm, the light reflex is actually decreased.

Gans⁴ recently explained in a simple and convincing manner why the light reflex is actually narrower in angiospasm and, at the same time, why it is wider in sclerosis. He cited Duke-Elder,⁵ who pointed out that in the normal fundus one sees the blood column only, and not the vessel, the wall of which is transparent. Gans cited Wilmer, Pierce

4 Gans, J. A. Classification of Arteriosclerotic-Hypersensitive Fundus Oculi in Patients Treated with Sympathectomy, *Arch. Ophthalmol.* **32**: 267 (Oct.) 1944.

5 Duke-Elder, W. S. *Text-Book of Ophthalmology*, London, Henry Kimpton, 1940, vol. 3, p. 2677.

and Friedenwald,⁶ who stated that the reflex stripe is produced by the reflection of light from the surface of the blood column and from the surface of the vessel wall. In normal arterioles the main source of reflected light is the surface of the blood column, as illustrated in figure 1*b* and *d*. He compared the light reflex of the normal arteriole to the light reflex from the surface of a penholder, showing that the light reflex is proportional to the diameter of the reflecting surface, as illustrated in figure 1*a*. When the arteriolar wall has undergone sclerosing changes, it is made optically denser, and its surface reflects proportionately more light, as illustrated in figure 1*c* and *e*.

A spasm seen in a normal arteriole is illustrated in figure 1*f*. Since the surface of the blood column is narrowed by the constriction of the arteriolar wall, the light reflex is also narrowed. Figure 1*g* represents a sclerosed arteriole the blood column of which has been narrowed by thickening of the vessel wall and intimal proliferation. Actually, in sclerosis the constriction is usually unsymmetric. The widened reflex at the site of narrowing of the blood column indicates that the thickened wall is producing most of the reflex and that the thickening of the arteriolar wall is greatest in this section.

CLASSIFICATION OF RETINAL ARTERIOLAR SPASM

For the convenience of description, the following classification of retinal arteriolar spasm in toxemia of pregnancy is suggested. The classification is based on the degree of arteriolar spasm and usually indicates the severity and duration of the toxemia.

GRADE 1—The spasms are localized and may be limited to one or more points. They are usually seen in the proximal portion of the arterioles. The general diameter ratio of vein to arteriole is the normal ratio of 3:2, or there may be a slight increase in this ratio.

GRADE 2—The arterioles show a generalized constriction so that the diameter ratio of vein to arteriole is 2:1. Usually there are also localized constrictions of the arterioles.

GRADE 3—The degree of generalized arteriolar constriction has increased until the diameter ratio of vein to arteriole is 3:1. Fine localized constrictions in the arterioles are usually present but are difficult to distinguish.

GRADE 4—The degree of generalized arteriolar constriction has progressed until the diameter ratio of vein to arteriole is 3:1 or more, and there is some degree of retinopathy. (Retinopathy will occasionally be seen in arteriolar spasm of grade 3, or even of grade 2, especially

⁶ Wilmer, W. H., Pierce, H. F., and Friedenwald, J. S. Light Streaks on Retinal Blood Vessels, *Arch. Ophth.* 9:368 (March) 1933.

if the localized constrictions are pronounced and the toxemia is sudden and severe)

ARTERIOLAR SPASMS SUPERIMPOSED ON ARTERIOLAR SCLEROSIS

Spastic arteriolar constrictions are often seen superimposed on chronic vascular disease, indicating that the existing toxemia of pregnancy has caused spastic constrictions of arterioles that previously had

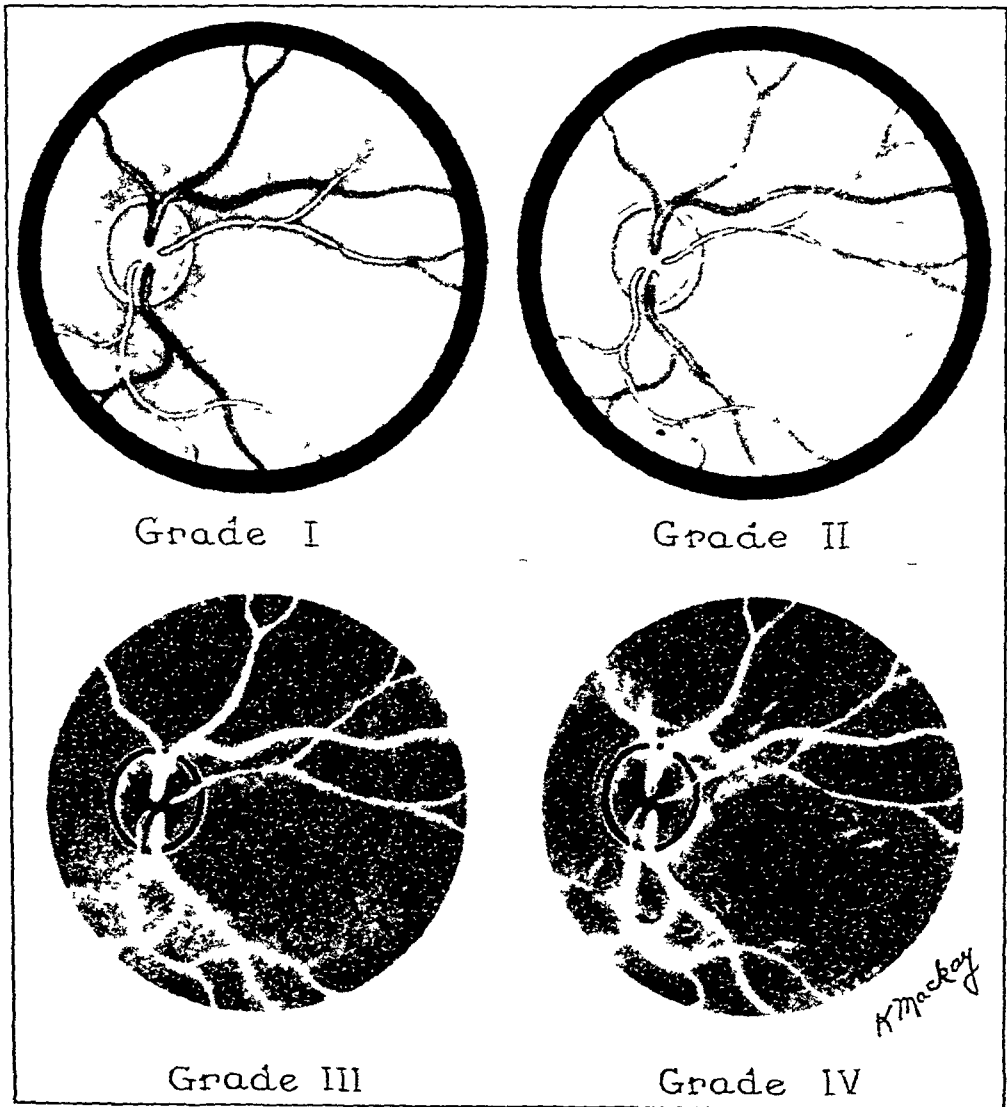


Fig 2 (Hallum)—Drawings illustrating classification of retinal arteriolar spasm (see text for details)

undergone sclerotic changes. When branches or portions of branches of the arterioles show constriction without an increase (or indeed with a decrease) in the light reflex it is likely that angiospasm is present.

Sclerotic changes are indicated by the usual signs of retinal arteriolar sclerosis, the most reliable being that of compression of the vein at the arteriovenous crossing. Unsymmetric constrictions of the lumen of the

arterioles, in contrast to the symmetric constrictions seen in angiospasm, are an indication of organic change in the arteriolar wall. The reflex stripe is an unreliable guide in estimating retinal arteriolar sclerosis, but when there is a marked increase in the light reflex stripe or when narrowed portions of an arteriole show an increase in the light reflex it is likely that there is vascular disease. Increased tortuosity of the arterioles is usually not seen until an advanced degree of arteriolar sclerosis has occurred, and then it is best seen in the terminal and very small arterioles. In a high percentage of such cases it is impossible on a single examination to be positive whether the changes are spastic or sclerotic in nature, or whether a combination of the two changes is present. If subsequent examinations, days, weeks or months later, reveal the disappearance of the arteriolar constrictions, it would be proof of their spastic nature, if the constrictions remain unchanged, or tend to increase, it would indicate permanent changes in the walls of the arterioles.

RETINOPATHY

As the retinal arterioles become more constricted there are seen signs of retinal ischemia, such as edema of the retina, hemorrhages and exudates. Edema of the retina is usually the first sign of involvement of the retina, and it generally makes its appearance at the upper and lower poles of the disk and progresses away from the disk along the course of the retinal vessels, which is likewise the general course of the nerve fibers of the retina. In the earliest stage of edema of the retina the portion involved appears milky, and on close examination with the very best focus of the ophthalmoscope, and with a gentle and slow to and fro rotation of the hand holding the ophthalmoscope, the surface shows faint striations running in the direction of the nerve fiber layers. As the edema becomes more marked, the retina becomes fluffy, grayish and semiopaque and tends to cover or surround the retinal vessels. In the presence of retinal edema it is difficult to judge the degree of arteriolar constriction.

The appearance of hemorrhages and exudates in the retina completes the picture of retinopathy. Some still prefer the name retinitis, and others prefer to call the condition retinosis. The hemorrhages are usually in the posterior one third of the fundus, and as a rule appear flame shaped, indicating that they are in the superficial nerve fiber layer. The exudates have a similar distribution and vary in size from that of a pinhead to half the area of the disk.

The recently formed superficial exudates, that is, the exudates in front of the retinal vessels, are whitish and fluffy and have hazy margins. After these exudates have been present for a few days, they become glistening white and the margins become more distinct. The exudates which form in the deeper layers of the retina, and possibly in the choroid, appear as indistinct grayish clouds. These changes in the retina usually

disappear completely after the termination of the toxemia and subsequent improvement in the blood supply to the retina

The earlier in pregnancy these toxic signs develop in the eyegrounds, the more serious is the prognosis. If retinopathy appears before the twenty-eighth week, there is only about a 25 per cent chance of the patient's giving birth to a live baby, even if the pregnancy is permitted to continue to the stage of viability. Wagener⁷ reported similar findings and cited similar observations of Schiøtz⁸ and Masters⁹.

DETACHMENT OF THE RETINA

In an occasional patient detachment of the retina will develop during severe toxemia of pregnancy. The detachment is usually bilateral and may or may not be accompanied with diffuse retinopathy. The detachment will usually become reattached spontaneously within ten to fourteen days after delivery. The portion of the retina that is detached is blind, but Benedict¹⁰ pointed out that as soon as it comes in contact again with the choroid it begins to "see." Eight or ten years ago, I thought that retinal detachment occurred in approximately 2 per cent of cases of hypertensive toxemia of pregnancy, but now I am convinced that this complication occurs much less frequently. Schiøtz⁸ found 7 instances of detachment among 158 cases of eclampsia and threatened eclampsia. Detachment of the retina complicating toxemia of pregnancy has been reported by many other observers¹¹.

FREQUENCY OF CHANGES IN THE EYEGROUNDS

In 1936 from a study of 16 of 300 consecutive patients with hypertension during pregnancy, it was found that the eyegrounds showed changes produced by the hypertension in 76 per cent. As shown in the

7 Wagener, H. P. Arterioles of Retina in Toxemia of Pregnancy, *J. A. M. A.* **101** 1380 (Oct 28) 1933, Lesions of Optic Nerve and Retina in Pregnancy, *ibid.* **103** 1910 (Dec 22) 1934.

8 Schiøtz, H. *Klin. Monatsbl. f. Augenh.* **67** 1, 1921.

9 Masters, R. J. Routine Ophthalmoscopic Examination as Aid in Management of Maternity Cases, *Tr. Am. Ophth. Soc.* **31** 416, 1933.

10 Benedict, W. L., in discussion on Kronfeld^{11g}.

11 (a) Blake, E. M. Bilateral Detachment of Retina in Nephritis of Pregnancy, *Arch. Ophth.* **51** 586 (Nov.) 1922. (b) Hill, E. Bilateral Detachment of Retina in Two Successive Pregnancies, *ibid.* **53** 137 (March) 1924. (c) Richardson, S. Case Report Bilateral Retinal Detachment Complicating Toxemia of Pregnancy, *J. Florida M. A.* **16** 266 (Dec.) 1929. (d) Black, N. M. Ocular Disturbance in Pregnancy and During Puerperium, *ibid.* **18** 121 (Sept.) 1931. (e) Crowther, W. L., and Hamilton, J. B. Eclampsia with Amaurosis Due to Detachment of Retinae, *M. J. Australia* **2** 177 (Aug 6) 1932. (f) Wagener⁷. (g) Kronfeld, P. C. Function of Reattached Retina, *Arch. Ophth.* **10** 646 (Nov.) 1933. (h) Jaffee, M. Retinal Detachment in Toxemias of Pregnancy. Report of a Case, *ibid.* **10** 454 (Dec.) 1933.

table, an increase in the frequency of the changes in the eyegrounds became apparent with an increase in the severity and duration of the hypertension. Class I includes the patients whose blood pressure before delivery was below 150 systolic and 100 diastolic, in class II are placed those patients whose blood pressure varied from 150 systolic and 100 diastolic to 175 systolic and 125 diastolic, and class III consists of the patients whose blood pressure was 175 systolic and 125 diastolic or more. Thus, it is seen that changes in the eyegrounds were found in 41 per cent of the patients in class I, in 84 per cent of the patients in class II and in 98 per cent of the patients in class III. Since these surveys were made, my colleagues and I have learned to give more attention to the presence of

*Relation of Positive Signs, Expressed as Percentages, and of Other Data to Severity of the Hypertension in a Series of Three Hundred Women with Hypertension During Pregnancy**

	Classes of Hypertension		
	I	II	III
Changes in eyegrounds	41.0	84.0	98.0
Retinopathy	3.7	9.9	32.7
Albuminuria	46.0	63.0	68.0
4 plus albuminuria	3.3	9.2	26.0
Casts in urine	7.6	20.0	26.0
Low output of phenolsulfonphthalein	43.8	41.8	45.2
Retention of nonprotein nitrogen			5.6
Abnormal gain in weight (last trimester, 40 cases)			7.5
First pregnancy	42.4	38.7	20.0
Sixth (or more) pregnancy	15.1	21.7	52.0
Average age	23.0	24.9	30.2
Labor induced	15.2	36.7	60.0

* After HALLUM.^{1b}

arteriolar constriction and to recognize even a single localized constriction. Now changes are found in the eyegrounds of approximately 100 per cent of the women who have pressures as high as 150 systolic and 90 diastolic for two or three days or longer.

Among other data, the table shows that albuminuria is often absent even in cases of severe toxemia and that the phenolsulfonphthalein excretion test is of no value with this condition. But it will be noted that the frequency of 4 plus albuminuria, casts in the urine and retinopathy is in proportion to the severity of the hypertension.

DIFFERENTIATION OF TYPES OF TOXEMIA

Interpretation of the changes in the eyegrounds often aids in differentiating the type of toxemia present. In preeclampsia and eclampsia the outstanding change is spastic localized and generalized constriction of the arterioles, and the degree of constriction usually is found to be

in proportion to the severity of the toxemia. When the angiospasm is severe, retinopathy appears.

Such spastic changes are found most often in the last trimester of pregnancy and are much more common in primiparas, especially young primiparas. This is because true toxemia occurs much more frequently in young women, especially during the first pregnancy. If the angiospasm did not exist long enough to cause organic changes in the walls of the arterioles throughout the body, the blood pressure returns to normal within a few days after delivery and remains so permanently, and the retinal arterioles soon resume their normal caliber. An increase in the uric acid content of the blood above 3.5 mg. per hundred cubic centimeters tends to indicate that the hypertension is of toxic origin, and peripheral resistance is actually produced by spasm of the arterioles. When the uric acid content of the blood is normal in a toxic patient who shows constriction of her retinal arterioles it is likely that vascular disease is the basis of the toxemia.

If the eyegrounds show only the signs characteristic of retinal arteriolar sclerosis, such as arteriovenous compression, unsymmetric arteriolar constrictions and increased light reflex, the hypertension is explained by vascular disease which antedated the present pregnancy. Vascular disease accounts for most cases of hypertension during the first two trimesters of pregnancy, and unless the hypertension is severe there are usually no toxic symptoms or positive laboratory findings. However, the hypertension of chronic vascular disease usually becomes accentuated during pregnancy.

Occasionally, angiospasm is superimposed on an eyeground showing changes characteristic of chronic vascular disease, indicating that pre-eclamptic toxemia is superimposed on chronic vascular disease. Such an ocular fundus will show arteriolar constrictions, localized and generalized, out of proportion to the evidence of vascular disease. It is usually impossible on a single examination to be positive of such a combination of changes, but if subsequent examinations reveal a decrease in the arteriolar constriction it is proof of the presence of angiospasm.

As emphasized by McCord¹² and Stander,¹³ the greatest factor in differentiating the various hypertensions of pregnancy is a long period of observation. The past history must be considered, together with repeated checks on the blood pressure, study of the eyegrounds, urinalysis, renal function tests, determinations of the uric acid content of

12 McCord, J. R. Premature Rupture of Membranes as Method of Inducing Labor, *Am J Obst & Gynec* **38** 587 (Oct) 1939.

13 Stander, H. J., in Williams, J. W. *Obstetrics Textbook for Use of Students and Practitioners*, ed 8, New York, D. Appleton-Century Company, Inc., 1941, p. 645.

the blood, etc. McCoid¹² gave Bartholomew credit for the following observation

A practical point that will often help in the differentiation of preeclampsia and chronic vascular disease is that bed rest, as a rule does not lower the blood pressure in preeclampsia but does lower the blood pressure in chronic vascular disease

I am not sure that I have ever seen an eyeground that indicated acute nephritis (acute glomerulonephritis) complicating pregnancy. This type of renal disease has a sudden onset and is characterized by marked edema, albuminuria, decreased renal function and subsequent hypertension. In acute nephritis of pregnancy one would expect to find the same changes in the eyegrounds that are found in acute nephritis from other causes, namely, retinopathy and in the early stages there would be an absence, or only a slight degree, of spasm of the arterioles. If the condition persists for several days or weeks, there will be seen to develop an increasing degree of angiospasm. Preexisting renal disease manifests itself in the eyegrounds only by the degree of generalized vascular disease that resulted from the previous nephritis.

Many patients with postpartum eclampsia have been examined, and most of them showed normal eyegrounds the first day or two after the sudden appearance of the severe toxemia. However, if the hypertension persists, within a few days there appear localized and generalized arteriolar constrictions, which tend to disappear as the hypertension subsides.

In March 1944, a questionnaire was mailed to the chiefs of the departments of obstetrics of the seventy-four grade A medical schools of the United States and Canada. The purpose of the questionnaire was to determine the frequency, and to learn the opinions concerning the relative value, of the study of the fundus oculi in the management of hypertension during pregnancy. Some of the facts learned from sixty-nine questionnaires which were answered follow:

- 1 Eighty-five per cent of the department chiefs feel that the information gained from the study of the eyegrounds helps in the management of hypertension during pregnancy.

- 2 Seventy-five per cent of the department staffs routinely study the eyegrounds of patients with hypertension during pregnancy.

- 3 Fifty per cent of the chiefs whose department staffs routinely study the eyegrounds of patients with hypertension during pregnancy rank the value of this information as of equal importance or as second in importance to the value of blood pressure determinations.

- 4 Forty per cent of the department staffs require the house officers, as part of their training, to study the eyegrounds of patients with hypertension during pregnancy.

Dr Henry P Wagener, of the Mayo Clinic, suggested that I check the findings of Suganuma,¹⁴ who compared the pressure in the brachial artery with that in the central retinal artery in patients with hypertensive toxemia of pregnancy. He made these determinations from one to four times on 10 patients, making a total of 20 determinations on the 10 patients. He listed several positive conclusions on the basis of his study of these 10 patients, and probably his most striking conclusion was that "in toxemia appearing in healthy primiparas an increase in retinal arterial pressure is the first appearing and probably the only inevitable sign of preeclampsia." When the retinal and brachial systolic and diastolic blood pressure readings in his cases are recorded graphically on the same chart, it is seen that there is a uniform tendency for the retinal arterial pressure to vary in proportion to the brachial arterial pressure.

Dr Wagener loaned me his Baillart ophthalmodynamometer, and I compared the brachial and retinal arterial pressures in 50 consecutive cases of toxemia of pregnancy. When my readings were recorded graphically on the same chart, they were, in general, similar to those of Suganuma, that is, the retinal systolic and diastolic pressures usually showed a general pattern in conformity with the brachial systolic and diastolic pressure. I was unable to find any consistent variations in the relationship of these graphs that might be characteristic of the severity or the type of toxemia. In general, I agree with Koch¹⁵ that individual ophthalmodynamometric readings alone are of no real clinical value in classifying patients with hypertension because the pressure in the central retinal artery varies too much in proportion to the pressure in the brachial artery.

REVIEW OF THE LITERATURE

Only four years after the invention of the ophthalmoscope by von Helmholtz, von Graefe,¹⁶ in 1855, first described the retinopathy of pregnancy. Silex,¹⁷ in 1895, reported the first large series, of 35 cases, and he expressed the belief that retinopathy occurred once in about 3,000 pregnancies. Miller¹⁸ found 6 patients with retinopathy in 1,800 pregnancies.

14 Suganuma, S. Studien über den Blutdruck in der Zentralarterie der Netzhaut, über den Blutdruck in der Netzhautarterie während des Verlaufes der normalen Schwangerschaft und der Schwangerschaftstoxikose, sowie über seine frühdiagnostische Bedeutung, *Klin Monatsbl f Augenh* **99** 637 (Nov.) 1937.

15 Koch, F. L. P. Retina in Systemic Vascular Hypertension. Clinical Study of Caliber of Retinal Arterioles and Retinal Arterial Diastolic Blood Pressure, *Arch Ophth* **26** 565 (Oct.) 1941.

16 von Graefe, F. W. E., cited by Cheney²⁰

17 Silex, P., cited by Cheney²⁰

Woods¹⁹ and Miller seem to have expressed the prevailing opinion up to about 1915 concerning the significance of retinopathy. Woods asserted that toxemia of pregnancy was the result of an unknown substance circulating in the blood and that this toxic substance was responsible for the changes observed in the eye, kidney and liver. He recognized that this substance produces thrombosis in many smaller vessels, with resulting degenerative changes in various parts of the body. Retinopathy, in his opinion, was an indication for promptly emptying the uterus, even in the absence of albuminuria.

Miller was the first obstetrician to attempt to correlate changes in the eyegrounds with the toxemia of pregnancy. He did his own ophthalmoscopy but had an ophthalmologist corroborate his findings in most cases. The outstanding point he stressed was that retinal lesions are found only with nephritic toxemia and that when nephritis is present in toxemia of pregnancy the renal lesion is primary and more or less extensive. In his opinion, retinopathy was not only an indication for immediate termination of the pregnancy but was also an indication for sterilization to prevent future pregnancies. Neither Woods nor Miller mentioned the status of the retinal arterioles.

In 1924, before the Section on Ophthalmology of the American Medical Association, Cheney²⁰ reviewed the literature and in a masterful manner correlated the obstetric and ophthalmologic point of view. His observations and conclusions were based largely on the newer concept of the cause of toxemia of pregnancy, namely, the contraction of the capillary and precapillary vessels, including those of the kidney. Volhard,²¹ according to Cheney, was among the first to state that retinopathy, and similar changes in other organs of the body, resulted from ischemia. Volhard claimed that the changes seen in the glomeruli in cases of nephritis were not a manifestation of an inflammatory process, but were simply an ischemic or asphyxial change secondary to a diminution of the blood supply. He found constricted arterioles in every case of retinopathy, and histologically the same vascular changes were observed in the renal vessels. Cheney cited Hewlett,²² who concluded that the action of a toxic substance caused the systemic arterioles to con-

18 Miller, J. R. Relation of Albuminuric Retinitis to the Toxemias of Pregnancy, *Am J Obst & Gynec* **72** 253, 1915

19 Woods, H. Ocular Complications of Pregnancy, *J A M A* **51** 204 (July 18) 1908

20 Cheney, R. C. Toxemias of Pregnancy from Ophthalmologic Standpoint, *J A M A* **83** 1383 (Nov 1) 1924

21 Volhard, J. *Ber u d Versamml d ophth Gesellsch*, 1916

22 Hewlett, A. W. *Pathological Physiology of Internal Diseases*, New York, D Appleton and Company, 1917

strict and thus produce hypertension. Silex, in 1895, mentioned narrowing of the retinal arterioles.

In a large number of toxemic patients at the Boston Lying-in Hospital, Cheney found narrowing of the retinal arterioles in most of those who had marked hypertension, and the constriction was dependent only on the hypertension, and not on whether the condition was acute toxemia or nephritis. He reasoned that in toxemia of pregnancy the vasoconstriction is sudden and retinopathy often develops because the retina does not have time to "compensate," or adjust to the diminished blood supply, whereas in arteriolar sclerosis of long standing the constriction of the arterioles is often more pronounced but the frequency of retinopathy is much less because the change is slow in developing and the retina has time to compensate. He expressed the belief that in the majority of cases one cannot differentiate between the acute toxemia and chronic nephritis by the fundus picture alone, because often the preexisting chronic nephritis was not severe enough to cause vascular changes visible with the ophthalmoscope but did produce sufficiently extensive changes to cause a flare-up of the nephritis from the extra burden of pregnancy. In his opinion, in such cases there is retinal angiospasm similar to the acute toxemia. In the discussion of this paper, Drs. Allen Greenwood, William C. Posey, Edward Jackson and Arnold Knapp expressed agreement in general with the conclusions.

It is generally considered that angiospasm can exist for several days at least without becoming fixed or sclerotic. Keith²³ stated the opinion that spasms might occur and leave no demonstrable injury, as illustrated by the angiospasm present in eclampsia, which is relieved by the termination of pregnancy, on the other hand, if the spasms persist, organic changes occur in the vascular walls and the kidney. He stated that angiospasm is capable of producing anemic infarcts. According to Freeman, Mylius²⁴ demonstrated by a series of fundus photographs that angiospasm is an indisputable fact. Bergmann cited the histologic examinations by Mylius²⁵ of the eyes of patients who had died in eclampsia and concluded that functional constrictions can exist for many weeks without becoming sclerotic.

Disturbance of vision during the acute stage of the toxemia is frequent. In approximately half the 47 cases of late toxemia reported by Schultz and O'Brien²⁶ visual disturbances were complained of. My

23 Keith, N. M. *Tr. Am. Acad. Ophth.* **30**:37, 1932.

24 Mylius, K., cited by Freeman, D. *Am. J. Ophth.* **16**:341, 1933.

25 Mylius, K., cited by Bergmann, M. B. *Relationships Between Ophthalmology and Obstetrics*, *Am. J. Ophth.* **17**:141 (Feb.) 1934.

26 Schultz, J. F., and O'Brien, C. S. *Retinal Changes in Hypertensive Toxemia of Pregnancy. Report of Forty-Seven Cases*, *Am. J. Ophth.* **21** 767 (July) 1938.

observation has been that vision is noticeably impaired when the retina in the macular region is edematous or when the macula is covered with hemorrhages or exudates. Vision in these situations is usually restored to normal or near normal when the toxic state is relieved. However, when detachment of the retina involves the macular region, the vision is seriously impaired at that time, and even after the retina is reattached the central visual acuity remains permanently impaired, often by as much as 50 per cent.

Masters,²⁷ in 1933, reported his findings in the routine ophthalmoscopic examination of 269 patients, beginning in many instances with the early prenatal visits. In 152 per cent of these patients slight retinal venous dilatation was present during the early months of pregnancy but disappeared by the eighth or ninth month. He found a generalized uniform constriction of the retinal arterioles in all patients whose systolic blood pressure was elevated to 150 mm of mercury. In 32 patients with severe toxemia, 10 out of 17 who had preexisting nephritis lost their babies, while only 4 out of 15 who did not have preexisting nephritis lost their babies. In his opinion, retinopathy is an urgent indication for termination of pregnancy, and mothers with retinal lesions in most instances will show permanent vascular and renal damage.

Wagener found spastic constriction of the retinal arterioles in about 70 per cent of women with hypertensive toxemia of pregnancy and considered it to be usually the primary sign of retinal involvement. In about 60 per cent of the patients the spastic lesions disappeared when pregnancy was terminated and the blood pressure returned to normal. In about 40 per cent of his patients organic lesions developed in the arterioles, and elevated blood pressure usually persisted. He did not consider retinopathy evidence of nephritis; instead, he stated that it indicated generalized arteriolar sclerosis. He showed by biopsy and at necropsy that the arterioles throughout the body were permanently damaged in patients with retinopathy and expressed the belief that the majority of them would have persistent hypertension.

Mussey²⁸ found that there was a definite increase in degree and severity of changes in the eyegrounds which was in proportion to the height and duration of the blood pressure. He asserted that the information gained from retinal examination is often a distinct aid in determining whether and when pregnancy should be terminated. He stated that examination of the eyegrounds early in pregnancy was of value in determining the presence of vascular disease, on which process might be seen the development of spastic lesions later in pregnancy.

27 Masters, R. J. Routine Ophthalmoscopic Examination as Aid in Management of Ninety-Three Maternity Cases, *Tr Am Ophth Soc* **31** 416, 1933.

28 Mussey, R. D. Relation of Retinal Changes to Severity of Acute Toxic Hypertensive Syndrome of Pregnancy, *Am J Obst & Gynec* **31** 938 (June) 1936.

Gibson²⁹ reported 39 cases of hypertensive toxemia of pregnancy, in 5 the eyegrounds were normal, in 20 they showed preorganic arteriolar constriction and in 11 they showed organic changes. He agreed essentially with my general conclusion, but I disagree with him on two points of observation.

1 He stated that in spastic arteriolar constriction there is an accentuation of the light reflex. According to my observation, the light reflex in this condition is not increased but has a tendency to be actually decreased. This is an important point in the differentiation of constriction produced by spasm from the constriction produced by sclerosis.

2 He further stated that localized constrictions usually are seen first in the extreme periphery of the retinal arterioles and that as the constriction increases the process involves the vessels closer and closer to the optic disk. My findings have been just the opposite, the localized constrictions usually first involve the proximal one third of the retinal arteriole and progressively spread toward the periphery of the arteriole. However, Duke-Elder³⁰ and Lillie,³¹ in their respective textbooks, have cited Gibson on these points.

According to Mussey and Mundell,³² the section on Obstetrics at the Mayo Clinic since 1921 has been using the changes in the eyegrounds, as a guide in the management of toxemia of pregnancy. The findings on retinal examination were a distinct guide to the management of approximately 28 per cent of the patients during the first five years of this period, of 51 per cent in the second five years and of 56 per cent in the last five years. They state:

The presence and degree of spasm of the retinal arteries has paralleled so closely clinical evidence of the severity of toxemia that we have increasingly depended on this examination.

Bartholomew and Colvin³³ presented the second study on hypertensive toxemia of pregnancy, based largely on the retinal examination, in which the ophthalmoscopic studies were done by the obstetrician. Miller reported the first study in 1915. Bartholomew and Colvin studied the eyegrounds of 286 consecutive patients throughout pregnancy and found that about one sixth showed slight to moderate arteriolar constric-

29 Gibson, G. G. Clinical Significance of Retinal Changes in Hypertensive Toxemias of Pregnancy, *Am J Ophth* **21** 22 (Jan) 1938.

30 Duke-Elder,⁵ p. 2724.

31 Smith, L. W., and others. Cardiovascular Renal Disease, New York, D. Appleton-Century Company, Inc., 1940, p. 14.

32 Mussey, R. D., and Mundell, B. J. Retinal Examinations. Guide in Management of Toxic Hypertensive Syndrome of Pregnancy, *Am J Obst & Gynec* **37** 30 (Jan) 1939.

33 Bartholomew, R. A., and Colvin, E. D. Interpretation of Blood Pressure Behavior During Pregnancy and Puerperium, *Am J Obst & Gynec* **42** 646 (Oct) 1941.

tion early in pregnancy, even though the blood pressure was normal. Two thirds of the patients showing early arteriolar constriction had hypertension during the last four to six weeks of pregnancy. About nine tenths of the latter group apparently had vascular disease, and none had severe toxemia. Only one fourth of the patients who showed normal arterioles during early pregnancy had hypertension during the last four to six weeks of pregnancy. True toxemia during the last trimester developed three times as frequently in the group showing normal arterioles during early pregnancy as it did in the group showing arteriolar constriction.

They compared the findings in the eyegrounds and the types of placental infarcts and found that usually both help to classify the toxemia. When the hypertension was due to vascular disease the eyegrounds usually showed evidence of arteriolar sclerosis, and the placenta, fixed in solution of formaldehyde U S P, usually showed white, or nontoxic, infarcts. When the hypertension was of toxic origin, the eyegrounds usually showed angiospasm and the placenta, fixed in solution of formaldehyde U S P, usually showed infarcts varying in color from yellow to brown and to black. The darkness of the infarct increased in proportion to the severity of the toxemia.

When hypertension is present during pregnancy without evidence of vascular or renal disease, the present consensus is that it is based on angiospasm. Addis³⁴ and Weiss³⁵ are among the most outspoken of the recent writers favoring this opinion. Many observers have seen spastic constrictions of the retinal arterioles during toxemia of pregnancy. Wagener found spastic constrictions of the arterioles in skeletal muscles taken for biopsy from patients with toxemia of pregnancy who at the same time showed spastic constrictions of the retinal arterioles. Hinselmann and associates,³⁶ according to Mussey, observed with the microscope recurring spasmodic constrictions of the arterioles in the nail fold of eclamptic patients.

Addis claimed that angiospasm produces the hypertension and explains all signs and symptoms of eclampsia. In the brain it produces hypertensive encephalopathy and excites convulsions, in the kidney it is responsible for albuminuria and oliguria, with a high specific gravity, in the liver it causes periportal necrosis, in the subcutaneous tissue it is responsible for anasarca, and in the skin it manifests itself by pallor.

34 Addis, W R. Pathogenesis of Eclampsia, *Brit M J* **1** 1103 (May 29) 1937.

35 Weiss, E. Practical Talks on Kidney Disease, Springfield, Ill., Charles C Thomas, Publisher, 1937, p 138.

36 Hinselmann, H, Neetekoven, H, and Silberbach, W. Capillary Circulation in Eclampsia, *Arch f Gynak* **116** 443 (Jan) 1923, abstracted, *J A M A* **80** 1108 (April 14) 1923.

Lyle³⁷ recently cited toxemia of pregnancy as a condition that occasionally produces encephalopathy

The after-effects of toxemia of pregnancy have been studied by many clinicians. Peckham³⁸ found that the frequency of chronic nephritis following eclampsia increased in proportion to the height of the systolic blood pressure. Nephritis did not develop if the systolic pressure did not exceed 170 mm of mercury, however, nephritis developed in 15 per cent of patients whose pressure reached 170 to 200 mm and in 48 per cent when the pressure exceeded 200 mm.

Herrick and Tillman³⁹ reported a series of 188 patients with mild toxemia of pregnancy, one third of whom showed hypertension one year or more later. Peckham and Stout⁴⁰ reported a similar series, one half of whom showed chronic vascular or renal disease five years later. Stander⁴¹ followed 800 patients, 35 per cent of whom had chronic nephritis, and 40 per cent of the latter had died in five to seven years.

Herrick and Tillman⁴² followed another large series of patients with toxemia of pregnancy and found that 80 per cent of the determinable deaths were of cardiovascularrenal origin. The mortality rate of this group was nearly seven times the average death rate for women of the child-bearing age. They found that 30 per cent of a group of patients who had non-nephritic hypertensive toxemia of pregnancy had a blood pressure of 150 mm at the end of the first year, and at the end of three years 50 per cent showed this degree of pressure, together with definite retinal arteriolar sclerosis.

CONCLUSIONS

The obstetrician should do his own ophthalmoscopy, because he will often gain invaluable information concerning the degree and severity of the toxemia, and without delay or extra expense to the patient. If this study is done only by the consultant ophthalmologist, he will be called in only once or twice in an occasional case of severe toxemia. At least 10 per cent of pregnant women show some degree of late toxemia,

37 Lyle, D. J. Association Between Retinopathies and Encephalopathies in Common Cardiovasculo-Renal Affections, *Am J Ophth* **27**:1232 (Nov.) 1944

38 Peckham, C. H. Chronic Nephritis Complicating Pregnancy, *Am J Surg* **35** 325 (Feb.) 1937

39 Herrick, W. W., and Tillman, A. J. B. Mild Toxemias of Late Pregnancy. Their Relation to Cardiovascular and Renal Disease, *Am J Obst. & Gynec* **31** 832 (May) 1936

40 Peckham, C. H., and Stout, M. L. Low Reserve Kidney, *Am J. Surg* **31** 92 (Jan.) 1936

41 Stander, H. J., cited by Norton, J. F., and Connell, J. N. Management of Toxemias of Pregnancy, *J. M. Soc. New Jersey* **33** 499 (Sept.) 1936

42 Herrick, W. W., and Tillman, A. J. B. Toxemia of Pregnancy: Its Relation to Cardiovascular and Renal Clinical and Necropsy Observations, with Long Follow-Up, *Arch Int Med* **55**:643 (April) 1935

according to Mussey⁴³, and, in the opinion of McCord,⁴⁴ chief of the obstetric staff where this study was made, the examination of the eyegrounds by one experienced in their interpretation gives the most information concerning the management and course of the various toxemias of pregnancy

It is now generally agreed that acute hypertensive true toxemia of pregnancy is characterized by localized and generalized spastic constriction of the arterioles, the degree of which has been found to parallel closely the severity of the toxemia. The degree of spasm of the retinal arterioles indicates the degree of angiospasm in other parts of the body. The eyegrounds should be examined routinely during the early months of pregnancy to determine the status of the arterioles, which will aid in the prognosis of the present pregnancy and will be valuable in interpreting changes that will be seen if toxemia appears later in pregnancy. When hypertension and other symptoms during late pregnancy indicate toxemia, the eyegrounds should be examined every few days, with special attention to the degree of angiospasm. When the degree of angiospasm increases in spite of conservative medical treatment, the pregnancy should be terminated to prevent permanent damage to the mother's vascular system. In some cases of toxemia the induction of labor is often a life-saving act for both mother and baby, and a study of the eyegrounds is probably the most consistently reliable single guide in determining when pregnancy should be terminated. On the other hand, the absence or scarcity of changes in the eyegrounds is often of great help in determining when it is safe to allow pregnancy to proceed.

478 Peachtree Street, N E

43 Mussey, R D. Significance of Retinal Changes in Toxemias of Pregnancy, *M Clin North America* **24** 1151 (July) 1940

44 McCord, J R. Conservative Treatment of Eclampsia. Study of One Hundred and Forty-Eight Cases, *J M Soc New Jersey* **34** 9 (Jan) 1937

OPHTHALMOSCOPIC CHANGES ASSOCIATED WITH HYPERTENSIVE VASCULAR DISEASE AS A GUIDE TO SYMPATHECTOMY

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NEW YORK

DURING recent years many articles have been published concerning the importance of fundic changes associated with benign and malignant essential hypertension (benign and rapidly progressive hypertensive vascular disease) ¹ These fundic findings will be discussed in relation to the surgical treatment of this prevalent disease Others will discuss the surgical and medical aspects

Essential Hypertension is regarded as a vascular disease of unknown etiology Its main clinical manifestation is a persistent high diastolic blood pressure, with variable general symptoms The disease often causes spasm or sclerotic thickening of the walls of the retinal chorioidal arterioles This results in narrowing or stenosis of the lumen, which frequently leads to pathologic changes in the surrounding area

Essential hypertension may be divided into two forms benign and malignant The benign form is a chronic disease, the malignant form is an acute disease Both forms occur mainly in adults Occasionally the benign form may become malignant, in which case fundic lesions are extensive

The fundic changes occurring with essential hypertension are varied Sometimes the fundi are normal for many years and no treatment

Read before the New York Academy of Medicine, Section of Ophthalmology, April 15, 1946

From the Department of Surgery of the New York Post-Graduate Medical School and Hospital (Columbia University)

1 Cohen, M Significance of Pathologic Changes in Fundus in General Arterial and Kidney Diseases, *J A M A* **78** 1694-1698 (June 3) 1922, Chorioretinal Arteriolar Necrosis in Malignant Hypertension, *Arch Ophth* **23** 1052-1058 (May) 1940 Gans, J A Classification of the Arteriosclerotic-Hypertensive Fundus Oculi in Patients Treated with Sympathectomy, *ibid* **32** 267-275 (Oct) 1944 Hinton, J W, and Lord, J W The Surgical Treatment of Advanced Hypertension, *New York State J Med* **1** 13-17 (Aug 20) 1945 Moritz, A R, and Oldt, M R Arteriolar Sclerosis in Hypertensive and Non-Hypertensive Individuals, *Am J Path* **15** 679-728 (Sept) 1937 Smithwick, R H Experiences with Surgical Treatment of Hypertensive Cardiovascular Disease of Man, *Cleveland Clin Quart* **12** 105-117 (Oct) 1945 Wagener, H P, Cusick, P L, and Craig, W M The Retina in Surgical Cases of Primary Hypertension, *Tr Am Ophth Soc* **37** 379-394, 1939 Peet, M M, Woods, W W, and Braden, S Surgical Treatment of Hypertension, *J A M A* **115** 1875-1885 (Nov 30) 1940 Woods, W W, and Peet, M M The Surgical Treatment of Hypertension, *ibid* **117** 1508-1515 (Nov 1) 1941

beyond general medical care may be required. At other times the fundi may show mild, moderate or severe lesions. For a time these changes may be stationary, progressive, regressive or remittent. A definite prognosis is not possible from the fundic findings alone, as it may be influenced by pathologic changes in other organs. Still, the eyegrounds are the best visible guide available to the condition of the systemic blood vessels, and therefore ophthalmoscopic findings afford an important prognostic indication in cases of essential hypertension.

Various systemic diseases may be accompanied with fundic lesions similar to those observed with essential hypertension. Accordingly, a physical examination should be made, and a clinical history and laboratory reports should accompany the fundic findings in order to establish a clinical diagnosis. Essential hypertension presents no pathognomonic signs, therefore, no definite correlation between the fundic findings and the unknown factor causing essential hypertension can be established.

Retinal lesions associated with benign essential hypertension are not inflammatory, hence, they are known as retinopathies or neuroretinopathies. Fundic lesions may be present in one or both eyes and may affect one eye more than the other. The acuity of vision will not be seriously involved unless the macular area or the visual field is affected.

Ophthalmoscopic diagnosis in cases of hypertensive disease requires a differentiation between arteriolar spasm and arteriolar sclerosis, which is an important but frequently impossible distinction. Some of the distinguishing fundic signs in spasm are retinal venous engorgement with tortuosity, narrowed arterioles, at times showing an uneven caliber, edema of the disk and retina, retinal hemorrhages and cotton wool patches, clinically recognized as exudates, and perivasculitis. These findings are usually transient and disappear with a period of absolute rest and the use of vascular dilators and sedatives.

If the narrowed arterioles are sclerotic, the vascular lesions are frequently permanent. The arterioles remain contracted, some have a "silver wire" central light reflex, while others are invisible, due to extreme contraction, or may be replaced by whitish lines, as in endarteritis. The venules are congested and tortuous and are compressed and deflected where crossed by sclerosed arterioles. There are retinal edema, hemorrhages and exudates. The exudates are usually resorbed in a short time, the glistening whitish dots or fatty degenerations remain for a long period.

Secondary hypertension will not be discussed, since it is caused by known primary disease entities, such as toxemia of pregnancy, pyelonephritis, chronic glomerular nephritis, tumor of the adrenal gland and arteriosclerosis. In cases of the secondary type treatment of the primary disease is necessary.

PRESENT STUDY

Through the courtesy of Dr J William Hinton, it was my privilege to examine the fundi of 90 patients with essential hypertension who were to undergo surgical treatment at the New York Post-Graduate Hospital. The fundi were examined frequently before and after operation over periods ranging from several months to two years. The findings were recorded and checked with other clinical data. Patients with severe organic disease were excluded.

Each patient was required to remain one or two weeks in the hospital prior to thoracolumbar sympathectomy in order to study the effects of rest and of the sodium amytal test on the diastolic pressure, as well as the data supplied by the physical examinations, including roentgenologic and electrocardiographic studies and laboratory tests of the blood and urine. If these reports proved satisfactory, the operation was performed in two stages at intervals of ten to fourteen days. For a detailed description of the operative technic it is necessary to consult surgical publications. Biopsies of small sections of the renal cortex were made at the second operation and were examined histologically.

According to my ophthalmoscopic findings, the fundi of patients with essential hypertension may be normal or the lesions may be classified as mild, moderate and severe. This is a tentative grouping and cannot be considered a hard and fixed distinction, as there are many borderline lesions. The results of successive examinations frequently determine their actual grading.

Of the 90 patients with essential hypertension, 86 revealed either normal fundi or mild or moderate fundic lesions, while 4 patients had severe lesions, such as occur with malignant essential hypertension.

Twenty-three patients had normal fundi, possibly because they were in an early stage of the hypertensive disease. One patient refused to undergo operation. The postoperative findings in the fundi of the remaining 22 patients continued to be normal. Microscopic examination of sections of the kidney showed normal structure in 3 patients, while 19 had mild or moderate nephrosclerosis of the interlobular renal vessels. Ophthalmoscopic examination served as a guide for sympathectomy in this group of patients, as it showed no evidence of the diffuse arteriolar disease, thereby suggesting a favorable prognosis. Sympathectomy was performed in order to relieve the severe subjective symptoms of these patients. The high diastolic blood pressure after sympathectomy was reduced in all but 2 patients in six months.

Fundic changes classified as mild were present in 43 patients. Most of these fundi showed a preoperative contraction of some arterioles with prominence of the central light reflex, the retinal veins were moderately engorged and tortuous, with compression over some arteriolar crossings, at times a few small hemorrhages and exudates were visible. One patient refused to undergo operation. Ten patients had normal fundi after operation, these fundi had shown spastic arteriolar lesions before operation. Thirty-two patients showed postoperative signs of arteriolar

sclerosis, consisting of a retinal residue of moderate venous engorgement, with local compression, and prominence of the central light reflex in the arterioles. These vascular changes were not reversible, but the edema, hemorrhages and exudates were resorbed after several days or a few weeks, contrary to similar lesions in cases of nonhypertensive diseases in which absorption occurs after longer periods. In all these patients biopsy of the kidney revealed mild or moderate nephrosclerosis. In this group of patients the ophthalmoscopic examination served as a guide for sympathectomy by the recognition of the early phase of the hypertensive vascular disease. Six months after sympathectomy the high diastolic blood pressure was greatly reduced in all but 5 patients. One patient in this group died of coronary disease two days after operation.

In the 20 patients with moderate fundic lesions before operation, the retinal arterioles showed a silvery white central light reflex, some venules were congested, with local compression and deflection, and there were slight edema of the disk, small edematous retinal areas, diffuse hemorrhages and exudates. One of the patients in this group refused to have an operation, and 1 was excluded because of organic disease. Two of the patients with preoperative angiospasm showed normal eyegrounds after operation, while in 16 there remained a residue of retinal arteriolar sclerosis. Within two days after operation 3 patients had fresh retinal hemorrhages and exudates, which, however, were transient. In this group with moderate hypertension the findings again indicated that the basic vascular lesions were not reversible, but the edema, hemorrhages and exudates were all resorbed. The sections of the kidney all indicated mild or moderate nephrosclerosis. In cases of moderate lesions of the eyegrounds, sympathectomy was indicated in order to prevent a possible progression to an advanced phase of the hypertensive disease. The high diastolic pressure in this group was greatly reduced six months after sympathectomy in all but 5 patients. Of 2 patients whose pressure was not reduced, 1 died of coronary disease four months and the other eight months after sympathectomy.

The fundic lesions in the 4 patients with severe, or so-called malignant, hypertension were extensive. The retina showed very severe lesions, as in the patients with moderate hypertension, there were massive areas of retinal edema with or without papilledema, profuse hemorrhages, a partial or complete star-shaped figure in the macular area, thromboses and exudates. These lesions signified the advanced phase of essential hypertension and generally indicated involvement of a vital organ. Two patients were not operated on because of concomitant organic disease. One patient died shortly after operation of a tumor of the adrenal, and 1 of coronary occlusion one month after operation. Biopsy revealed malignant nephrosclerosis of the kidney in 1 of the patients undergoing operation and moderate vascular involvement in

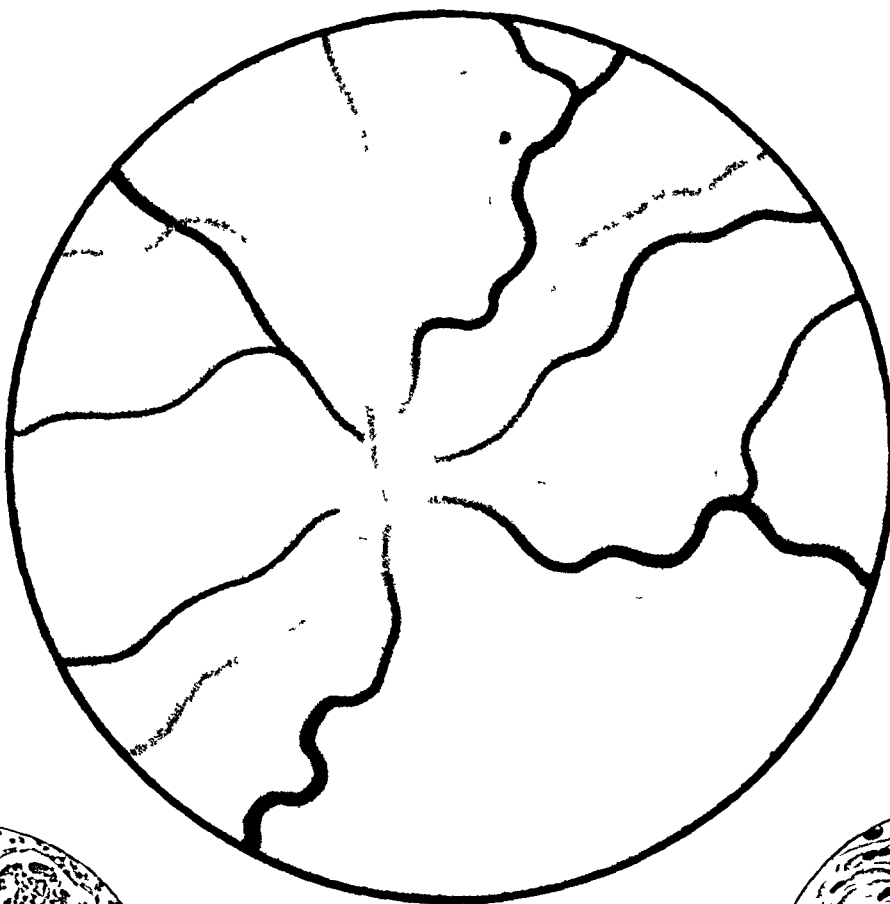


Fig 1



Fig 3



Fig 4

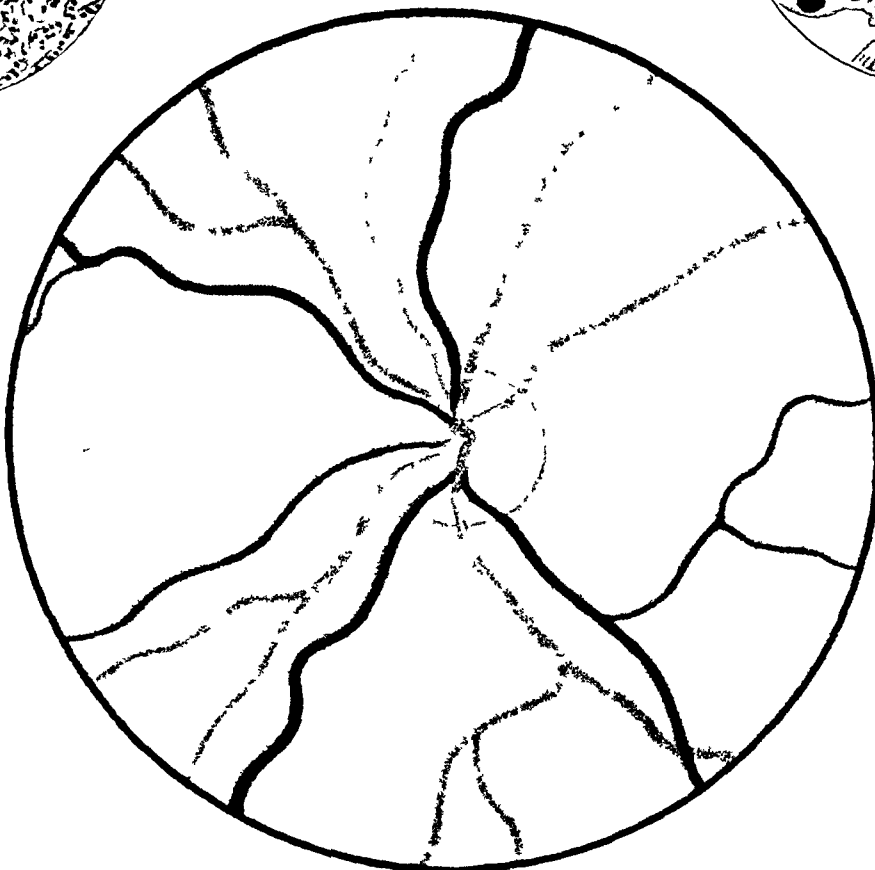


Fig 2

- Fig 1 Before Sympathectomy
 Fig 2 Three weeks after Sympathectomy
 Fig 3 Kidney Section (Low Power)
 Fig 4 Kidney Section (High Power)

the other. From an ophthalmoscopic standpoint, sympathectomy in cases of severe hypertension would be advisable only if the patient insisted on it because of suffering from severe subjective symptoms which medical treatment could not alleviate.

In this connection, I have reported a case of so-called malignant essential hypertension with severe fundic lesions in which death was due to cerebral hemorrhage. Pathologic study demonstrated necrosis of the arteriolar wall of the retina and choroid and hyperplastic arteriolar sclerosis in all the organs, as verified by autopsy. I have observed a few patients with severe fundic lesions associated with malignant hypertension for several years; they lived from two to eight years without surgical intervention. However, satisfactory results have been reported after sympathectomy in cases of malignant hypertension with severe fundic lesions.

It is important to note that in the majority of the 90 patients the progression of clinical manifestations of the hypertensive disease was reflected in progression of the fundic lesions. The association of the fundic findings with renal arteriolar sclerosis is significant; it was manifested in 96 per cent of the patients operated on. This fact requires further investigation as to prognosis.

The following case is 1 of several in which the ophthalmoscopic findings served as an important guide to thoracolumbar sympathectomy.

REPORT OF A CASE

L. D., a man aged 34, white, single, was a newspaper deliverer. His family history was irrelevant, and he had been in perfect physical health until 1941. At this time his draft board diagnosed his physical condition as idiopathic hypertension. He then was treated by his family physician for this ailment for two years. Medical treatment was of no avail in relieving his symptoms. His blood pressure gradually rose to 250 systolic and 150 diastolic, and he had excruciating headaches and other subjective complaints. He was referred to Dr. Maurice Bruger, who, in turn, suggested that he be admitted to the New York Post-Graduate Hospital for sympathectomy. On his admission in June 1943, the nonprotein nitrogen was 35 mg., and the urea nitrogen 17.5 mg., per hundred cubic centimeters; the test for urea clearance, as well as other tests, gave normal results. Examination of the fundi showed a moderate form of neuroretinopathy (fig. 1).

He was admitted to the hospital, and after a two week period for preliminary examinations, the results of which were satisfactory, a thoracolumbar sympathectomy was performed by Dr. J. William Hinton. Postoperative results were satisfactory; his blood pressure was reduced to an average of 150 systolic and 100 diastolic, his headaches disappeared completely, and he was able to resume his work after an absence of five months. For a period of two years his condition has remained satisfactory, and he is at present in perfect health.

He has had periodic ophthalmoscopic examinations for the past two years. Postoperative examinations of the fundi showed resorption of all retinal lesions, with a normal vasculature after three weeks (fig. 2). The angiospastic condition

which existed prior to operation was relieved. No evidence of angiosclerosis was seen at any time in the fundi. Biopsy of the kidney revealed mild nephrosclerosis, demonstrating hyaline thickening of the intima and media of the arterioles (figs 3 and 4). This case exemplifies the beneficial and satisfactory results obtained from thoracolumbar sympathectomy.

SUMMARY AND CONCLUSIONS

In 82 patients with benign essential hypertension (hypertensive vascular disease) no progression of the retinal lesions was observed after sympathectomy.

Of 60 patients with associated hypertension with mild or moderate fundic lesions, regression of the retinal hemorrhages, exudates and edema were observed in 22 after sympathectomy, but the basic underlying retinal arteriolar sclerosis remained unchanged in 48. Retinal angiospasm was relieved in 12 patients. Further study is required to determine the significance of this retinal residue.

Cases of benign essential hypertension, showing normal eyegrounds or mild or moderate fundic lesions, are suitable for sympathectomy if continued medical treatment is of no avail in alleviating the severe and persisting subjective symptoms.

The group of patients who had so-called malignant (rapidly progressive) hypertension with extensive fundic lesions was too small to call forth any comment. An adequate series of such patients should be studied from an ophthalmoscopic standpoint.

Finally, the purpose of sympathectomy is the relief of subjective symptoms of patients with essential hypertension. The advisability of sympathectomy is determined primarily by the internist, whose decision is based on the consideration of all clinical data in essential hypertension.

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KERATOCONJUNCTIVITIS DUE TO A DIPHATHEROID-LIKE ORGANISM

Report of a Case

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AND
D LOCATCHER-KHORAZO, M D
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NUMEROUS organisms and infectious agents have been implicated in keratoconjunctivitis. The following case illustrates a severe type of infection produced by an organism of the diphtheroid group.

REPORT OF CASE

History—M A V, a 26 year old unmarried white woman, was first seen at the Institute of Ophthalmology on March 21, 1944, with the following history. At the age of 7 she had an attack of scarlet fever, which left her eyes sensitive to light for about one year. There was, however, no other ocular complaint until six years prior to the first examination, when, rather suddenly, severe blepharoconjunctivitis developed in both eyes. This condition was treated with drops by several doctors, and there were numerous exacerbations and remissions. There was considerable purulent discharge, and the patient stated that the margins of the lids remained red and irritated. In 1940 she noted a decrease in visual acuity, especially in the right eye. There was increased sensation of irritation, the eyes were acutely inflamed, and she was told that her corneas were scarred. At the same time she began to be troubled with trichiasis, for which frequent epilation was necessary. There was no history of a diagnosis of trachoma having been made, nor was there any history of physical illness.

Examination—Vision was 3/200 in the right eye and 20/70 in the left eye with and without correction. She was wearing + 3.00 D cyl, ax 95 for the right eye and + 0.50 D sph \cap -2.50 D cyl, ax 5 for the left eye. There was considerable injection of the bulbar conjunctiva, especially at the inner canthus. The normal mucocutaneous juncture of the lids was obliterated and was replaced by scar tissue, containing a large number of aberrant cilia, especially on the lower lids. This scar tissue was about 4 mm wide and extended as a ragged edge over onto the conjunctival surface of the lids. There was redness and roughening of both the upper and the lower fornix, with papillary hypertrophy. In the regions of the upper tarsus were some follicles and a minimum amount of scarring.

Examination of the right eye with the corneal microscope revealed a thin vascularized membrane over the entire cornea with small areas of calcification in the center (fig 1). There was some punctate staining around the calcified areas. The left eye showed considerable punctate staining with fluorescein and an

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area of vascularization invading the limbus 2 or 3 mm and extending clockwise from 6 to 2 o'clock. The border of this area did not stain, however.

The tension of the two eyes was normal to finger palpation. Ophthalmoscopic examination was unsatisfactory in the right eye because of the corneal opacification. The left fundus was normal.

The appearance of the eyes suggested an eczematous (scrofulous, phlyctenular or lymphatic) conjunctivitis with associated corneal changes and an old ulcerative blepharitis with no phlyctenules present now. The pannus also suggested this diagnosis rather than that of trachoma, since the vascularization was not confined to the upper portion of the cornea.

General examination revealed a somewhat undernourished condition. Studies of the blood revealed a hemoglobin concentration of 73 per cent and a red cell count of 3,570,000. The white cell count was 5,000, with 57 per cent polymorphonuclear cells and 40 per cent lymphocytes. She was given vitamin B complex, oral liver extract and elixir of a proprietary hematinic preparation (Feosol). Under this treatment her appetite improved and she felt stronger.

Cultures were taken of the eyes, and epilation was done. She was given an ointment containing sodium sulfathiazole, 5 per cent, to instill in the eyes three times a day.

LABORATORY STUDIES

Morphologic Characteristics—Cultures taken from the conjunctivas and lids of both eyes revealed a pure culture of a gram-positive bacillus which was isolated from aerobic and anaerobic conditions. Direct smears from the conjunctivas showed a moderate number of gram-positive, diphtheroid-like organisms with short and long forms. Also present were a moderate number of polymorphonuclear leukocytes and a few epithelial cells. No inclusion bodies were observed in epithelial scrapings stained with the Giemsa stain. The diphtheroid-like organisms showed considerable pleomorphism. Some were in the form of parallel rods, others had club-shaped ends. No capsule was observed. Granules were noted and were more prominent when stained with methylene blue. The organisms were nonmotile and non-acid-fast. A few staphylococci were also present which did not ferment a phenol red (phenolsulfonphthalein)-mannitol agar plate.

Cultural Characteristics—Growth was obtained on ordinary mediums of material taken directly from the eye. On plain agar the colonies developed gradually from 1 to 5 mm after seventy-two hours' incubation at 37 C. The optimum temperature for growth was 37 C, but the bacteria grew at room temperature. In older cultures, after four to five days, a yellow pigment developed. The colonies appeared rough, irregular and dry, with grayish margins and yellow centers (fig 2). They were not convoluted and were easily dislodged from the medium. The same morphologic features were noted on a rabbit blood agar plate, and there was no hemolysis. On potato medium a scant growth was obtained in forty-eight hours. In liquid mediums after twenty-four hours a pellicle formed, which broke up into small flakes. This pellicle was yellow.

Resistance—The culture survived without subculturing for about nine months. Broth cultures heated at 56 C for one hour produced no growth.

Biochemical Reactions—The organisms produced acid without gas with dextrose, maltose, sucrose, levulose and xylose. With raffinose acid was produced in twenty-four hours, but the reaction was reversed to neutral after forty-eight hours. No acid or gas was produced with salicin, dulcitol, mannitol or lactose (table 1). In litmus milk a very slight acidity was produced after incubation.

for one week. No coagulation or digestion occurred after incubation for two weeks. Gelatin and Löffler's medium were not liquefied. The methyl red test gave a negative reaction, and no indol or hydrogen sulfate was produced. Nitrites were not formed.

Animal Inoculation—An emulsified culture of the isolated bacillus was prepared and the following animal inoculations were carried out:

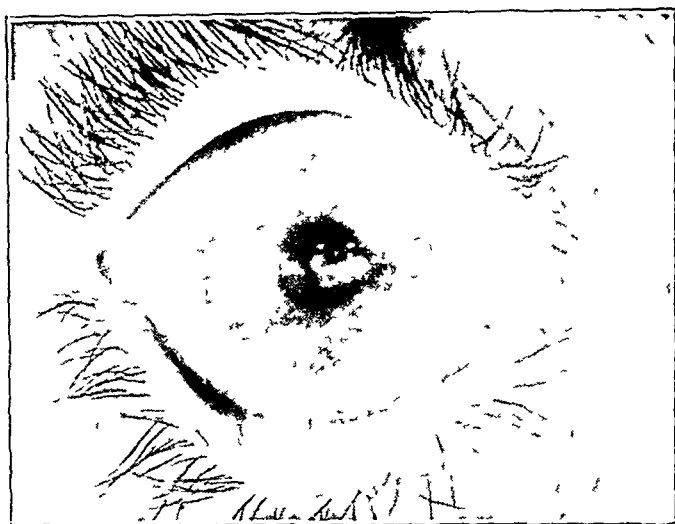


Fig. 1—Vascularized membrane covering cornea, with areas of calcification.

Mouse—An intraperitoneal injection of 0.3 cc of the emulsified broth culture was made, using an adult white mouse. No effect was produced in two weeks.

Guinea Pig—An intraperitoneal injection of 0.3 cc was made, with no effect.

Rabbit—An adult white rabbit was used for intraocular studies. The right eye was given a subconjunctival injection of 0.05 cc of the broth culture,

TABLE 1—*Biochemical Reactions of Fermentation Sugars*

Fermentation Sugars	Acid	Gas
Dextrose	+	0
Maltose	+	0
Sucrose	+	0
Levulose	+	0
Raffinose	+	0
Xylose	+	0
Salicin	0	0
Dulcitol	0	0
Mannitol	0	0
Lactose	0	0

the point of injection being just above the limbus at 12 o'clock. The following day the entire cornea was greatly injected, and there was a purulent discharge containing the organisms. At the end of a week the conjunctival reaction subsided, but there was now a beginning vascularization of the cornea above and below (fig. 3A).

An injection was made in the other eye of the same rabbit, using 0.02 cc of the emulsified broth culture, the injection being made through the cornea into

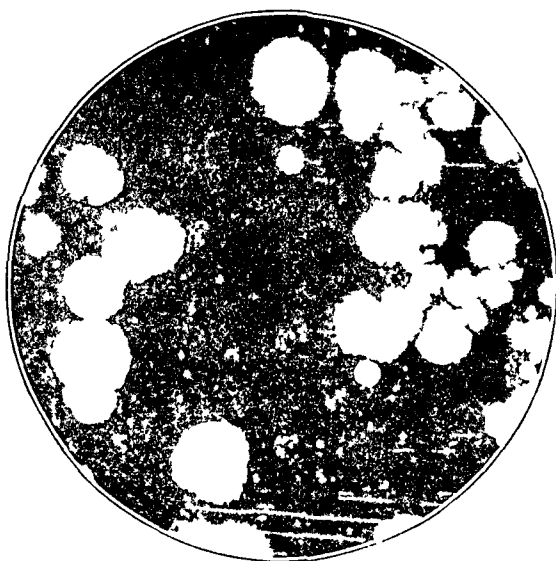


Fig 2—Colonies of *Corynebacterium xerose* four to five days old

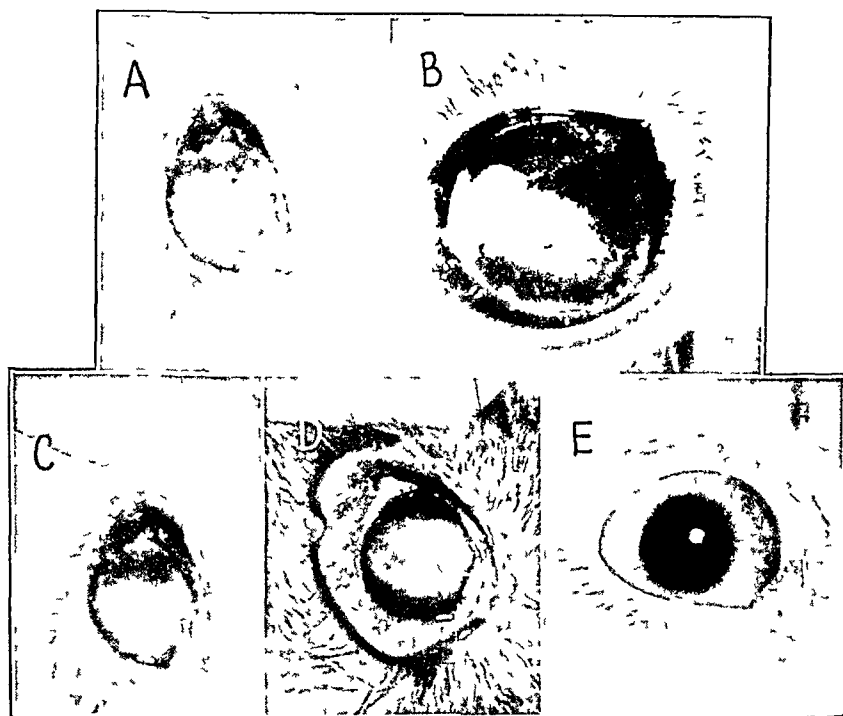


Fig 3—Rabbit eyes after injection of a broth culture of the diphtheroid organism taken from the eye shown in figure 1. *A*, beginning vascularization of the cornea one week after subconjunctival injection of 0.05 cc of the broth culture just above the limbus, *B*, opaque, vascularized cornea about three weeks after injection of 0.02 cc of the broth culture into the anterior chamber of the other eye of the same rabbit, *C*, cloudy cornea of a second rabbit twelve days after injection into the anterior chamber of 0.04 cc of another broth culture of the organism, *D*, complete opacification of the cornea and conjunctivitis in a third rabbit two weeks after injection into the anterior chamber of 0.02 cc of the same culture as that given the second rabbit, *E*, rabbit eye into which a plain sterile broth was injected, as a control.

the anterior chamber. The following day the conjunctiva was found to be greatly congested, with purulent discharge. The anterior chamber was reformed, the cornea was somewhat translucent, and the tension was normal to finger palpation. Four days later a thick exudate was noted in the anterior chamber. At the end of a week the cornea was hazy. At the end of two weeks the conjunctival reaction had subsided. The cornea was now completely opaque and vascularized (fig 3 B). Tension as taken with the fingers appeared low. There was no change in appearance at the end of three weeks. Another rabbit received an injection of 0.04 cc of another broth preparation of organisms into the anterior chamber. At the end of eight days a pannus had formed from above, and there was considerable reaction in the conjunctiva, which subsided at the end of twelve days, leaving a cloudy cornea (fig 3 C).

An additional rabbit was given an injection of 0.2 cc of the same broth culture. The following day there was a severe purulent conjunctivitis containing the same organisms, as well as staphylococci. At the end of two weeks there was complete opacification of the cornea, with considerable conjunctivitis still remaining (fig 3 D). Tension as taken with fingers was low.

Scrapings were taken from the lower lids on Jan 30, 1946 and placed in a test tube of saline solution. An injection of 0.02 cc was made in the anterior chamber of a rabbit. The effect produced was similar to that shown in figure 3 C.

Two rabbits received injections of 0.02 cc of saline solution and broth, respectively, in their right eyes. No effect was produced. Figure 3 E shows the rabbit's eye after injection with plain sterile broth.

Monkey. A few drops of a broth culture of the organisms was instilled in the right eye of a *Macacus rhesus* monkey. The following day there was a slight redness of the conjunctiva, which disappeared within twenty-four hours.

Clinical Course.—The patient was advised to use sodium sulfathiazole ointment, five per cent, three times a day, and epilation was done at intervals of two weeks to cut down irritation to the cornea. In addition, she received an extract of liver and iron by mouth and was placed under the care of an internist. The cornea ceased to stain after two weeks, and vision improved.

On Oct 19, 1944 vision in the right eye was 20/200—, not improved, and in the left eye was 20/30, corrected to 20/20-1 with a +0.25 D sph \ominus 2.50 D cyl, ax 15. Examination with the slit lamp showed considerable clearing of the left eye but with the vascularization and calcified deposits remaining. The left eye showed thinning of its vascularized area. There was no staining of either eye after two weeks of treatment. On March 1, 1945 the hemoglobin had risen to 92 per cent and the red cell count had reached 4,355,000.

Cultures have remained positive in spite of the clinical improvement. Penicillin ointment has been tried, and at present the patient uses this twice a day and alternates with the sodium sulfathiazole ointment at monthly intervals. There are fewer abnormal cilia now, and the patient has less irritation as long as she continues to use local applications of ointment to the eyes. Vision in the right eye is now corrected to 20/100 with +3.00 D cyl, ax 95, and vision in the left eye is 20/20 with the previous correction.

Cultures from both eyes still produce heavy growths of the organisms in spite of local chemotherapy. There continue to be considerable injection and roughening of the conjunctival surfaces of the lids.

CONCLUSIONS

In view of our bacteriologic studies, we feel that the etiologic factor in this case is the diphtheroid-like organisms which we have isolated in pure culture. Biochemical reactions would place it with the diphtheroid type of the *Corynebacterium* group (table 1). A comparison of this organism with other diphtheroids (table 2) would lead one to consider it in the *Corynebacterium xerose* group. The fact that the organism was nonpathogenic for mice and guinea pigs would rule out the possibility of its being *Corynebacterium pseudotuberculosis ovis* (of Preisz and Nocard) or *Corynebacterium pseudotuberculosis murium*, both of which produce systemic effects when injected intraperitoneally into such animals. It could be a form of *Corynebacterium flavidum*, which is found in the nose and throat and which also occurs in the udder of cows with mastitis.

TABLE 2—*Differentiation of the Various Forms of Corynebacterium*
(Adapted from Topley and Wilson)

	Fermentation of Sugar						Liquefac- tion of Gelatin
	Dex- trose	Mal- tose	Saccha- rose	Dex- trin	Lac- tose	Man- nitol	
<i>C. diphtheriae</i>	+	+	—	+	—	—	—
<i>C. diphtheriae</i> (avirulent)	+	+	—	+	—	—	—
<i>C. hoffmanni</i>	—	—	—	—	—	—	—
<i>C. xerose</i>	+	+	+	—	—	—	—
<i>C. pyogenes</i>	+	+	±?	—?	±	—	±
<i>C. renale</i>	+	—	—	—	—	—	—
<i>C. ovis</i>	+	+	—	±	—	—	+
<i>C. murium</i>	+	+	+	—	—	—	—
<i>C. acnes</i>	+	+	±	—?	—	+	—
<i>C. typhi</i>	+	+	—	—	—	—	—

During the past fifty years considerable work has been done in an attempt to prove the pathogenicity or nonpathogenicity of *C. xerose*. Frankel and Franke¹ in 1887 injected material containing *C. xerose* organisms into the anterior chamber of the guinea pig and instilled the same material into the conjunctival sac of 5 human subjects, with no untoward results. Weeks² in 1887 made a study of the xerosis bacillus in infants and children and came to the conclusion that no pathologic change was produced.

Bietti³ in 1903 carried out studies in which he inoculated the eyes of several of his colleagues, with no ill effects. Andrewes, Bulloch and

1 Frankel, E., and Franke, E. Ueber den Xerosebacillus und seine aetiologische Bedeutung, Arch f Augenh **17** 176-192, 1887.

2 Weeks, J. E. Xerosis conjunctivae bei Sauglingen und bei Kindern, Arch f Augenh **17** 193-202, 1887.

3 Bietti, A. Welche Bedeutung kommt den Diphtheriebazillen und verwandten Keimen in der Aetiologie der einfachen Bindehautentzündungen zu? Klin Monatsbl f Augenh **41** 87-124, 1903.

others ⁴ reported a series of studies in 1923 with the same results. Gay,⁵ Topley and Wilson⁶ and Duke-Elder⁷ all stated that there is no adequate evidence that the diphtheroids are pathogenic for the eye.

It is our feeling that the organism isolated in this case is a diphtheroid. In spite of statements to the contrary, it would seem as though this organism was pathogenic. This is especially true since no organisms of the *Haemophilus* group were found in the patient's eyes. The point might be raised that there is a history of poor physical condition, such as might cause nutritional changes in the cornea. In view of the improvement in the patient's physical condition and the continued infection with exacerbations and remissions, we feel that the organism described has a direct relationship to the keratoconjunctivitis.

SUMMARY

A stubborn case of keratoconjunctivitis with blepharitis and trichiasis is presented in which a pure culture of a diphtheroid-like organism was isolated.

Dr Martin Frobisher, of Johns Hopkins University, and Dr Harry E. Martin, of the University of Pennsylvania, assisted in identifying the organisms isolated in this case.

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4 Andrewes, F. W., and others. *A System of Bacteriology in Relation to Medicine*, Medical Research Council, London, His Majesty's Stationery Office, 1923, p. 380.

5 Gay, F. P. *Agents of Disease and Host Resistance*, Springfield, Ill., Charles C. Thomas, Publisher, 1935, pp. 948-951.

6 Topley, W. W. C., and Wilson, G. S. *The Principles of Bacteriology and Immunity*, Baltimore, William Wood & Company, 1936, pp. 346-551.

7 Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1941, vol. 2, pp. 1467-1468.

SENSORIAL RETINAL RELATIONSHIP IN CONCOMITANT STRABISMUS

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(Continued from Page 368)

III CLINICAL PICTURE OF ANOMALOUS RETINAL CORRESPONDENCE AND ITS INTERPRETATION

The normal relationship between the two retinas, the normal retinal correspondence, is based anatomically on the interrelation between the cells of the sensory epithelium of the retinas and the cells of the visual sphere of the brain cortex. Ample experimental evidence has shown that the normal retinal relationship is physiologically fixed and that it cannot be altered in a subject with normal binocular vision. Yet anomalous correspondence does exist and can be observed daily in the practice of every ophthalmologist.

How can this apparent contradiction be explained? The supporters of the so-called empiristic theory of space perception found an easy solution to this problem and, indeed, perceived one of the foundations of their doctrine in the fact that squinting persons are capable of acquiring a retinal relationship which differs from that of nonsquinters. They reasoned that the faculty of localizing bifoveal stimuli in the same direction is learned and acquired in the early stages of individual life. However, such a type of localization is useful only if the visual lines intersect at the point of fixation. If there is a deviation of one of the visual lines, that is, if there is a strabismus, the patient makes up for the motor anomaly by learning how to localize in the same relative direction a stimulus impinging simultaneously on the fovea of one retina and on an eccentric element of the other retina, i.e., he acquires anomalous correspondence.

The empiristic theory has been superseded by the nativistic theory, according to which the normal retinal correspondence is innate or acquired through phylogenetic, rather than individual, experience. Every one is born with such a distribution of the relative directional spatial values of the retinal elements that the two foveas are corresponding elements. This condition is, indeed, fixed and immutable.

It is of interest to recall in this connection Lorente de Nó's theoretic consideration of the point to point relationship between the retina and

the cerebral cortex in the region of the calcarine fissure³⁹ Owing to the extensive arborization, each element of the retina is connected with a large area of the cortex, and each impulse set in any point of the retina could, therefore, be transmitted to a large area of the cortex This overlapping of the nerve paths would make a point to point projection of the retina in the optic centers impossible if the theory of "avalanche conduction" of Ramón y Cajal and Herrick were correct Lorente de Nó did not accept this theory He considered the anatomic mechanism to be only potential and expressed the belief that, owing to the high threshold of the neurons, only a limited number of the anatomically possible transmission paths are accessible to afferent impulses The role of the central stations would thus consist in concentrating the stimuli in a few conductors, rather than in increasing the number of active conductors Physiologically, therefore, a point to point projection is possible, provided that the nerve cells have a sufficiently high threshold and are made to discharge only when a large number of their synapses are active

It would, however, show a lack of biologic and physiologic understanding if one were to assume that a rigid anatomic point to point relationship between the elements of the two retinas would entail an equally rigid physiologic relationship

The retina is ontogenetically, structurally and functionally a part of the brain The prime function of the central nervous system is to correlate and integrate the activities of the organism into a purposeful unit A rigid immutability, such as is necessary for the functioning of the peripheral organs, would defeat the purpose of the central nervous system Its purpose is to adjust the function of the different organs and their parts in such a way as to meet the external and internal conditions present at a given moment, it must reintegrate their function if the integration is at fault or endangered This coordinative, integrative action of the central nervous system (Sherrington⁴) is the basis of the adaptability of the human organism

The fixed normal correspondence does not imply a true point to point relationship of the retinal elements This would not be expedient and is not assumed in the classic writings on retinal correspondence Johannes von Muller's old theory of the identity of the corresponding elements might, to be sure, imply such a relation, but it has long since been abandoned It is known from Panum's investigations that the elements of each retina correspond physiologically not to one element of the other retina, but to a group of elements occupying an area of measurable dimensions It is of importance to know that the size of

39 Lorente de Nó, R Studies on the Structure of the Cerebral Cortex
II Continuation of the Study of the Ammonic System, *J of Psychol u Neurol*
46 113, 1934

these areas is not absolutely fixed. Their dimensions are relative ones and can be somewhat reduced by training.⁴⁰

If there is a change in the normal motor relation between the two eyes, the normal sensorial correspondence no longer serves a useful purpose, in fact, it becomes detrimental. An adjustment takes place, and a new sensorial relationship between the elements of the two retinas appears. But one must always keep in mind that the normal retinal relationship is not irretrievably lost, it remains potentially—and sometimes even actually—present, it has only given way to a new relationship, which, in turn, may be replaced if it is no longer adequate.

The anomalous sensorial relationship between the two retinas, the anomalous retinal correspondence, represents, thus, a process of adaptation of the sensorial to the anomalous motor conditions, it consists in a shift of the visual directions of one eye relative to those of the other eye.

But one cannot exact from anomalous correspondence the same accuracy as from normal correspondence. It must again be stressed that anomalous correspondence is nothing but an attempt of the organism to adapt the sensorial to the motor conditions, an attempt which is not always successful. And even where it is most successful—as in patients who in the clinical tests show an anomalous correspondence adapted to the angle of squint—refined laboratory methods may disclose considerable inaccuracies in the new sensorial relation of the two retinas. This is only to be expected, given the nature of anomalous correspondence, if one loses sight of its nature, one is apt to draw from laboratory experiments fallacious conclusions about the essence of the condition.

Not in all patients with concomitant strabismus does anomalous correspondence develop. The conditions which are necessary to bring this about must now be considered.

The first prerequisite is a certain amount of binocular cooperation. I have shown in an earlier paper that anomalous correspondence does not appear in patients whose binocular cooperation prior to the onset of the strabismus was restricted to the presence of the primitive, rudimentary visual directions.¹⁵ The *raison d'être* of anomalous correspondence is the binocular cooperation, and it can arise only if the eyes are, at least at times, used together. In cases of definite alternating strabismus, in which the patient is able to change fixation at will from one eye to the other and in which there is habitually alternating unocular vision, one therefore finds normal correspondence frequently, even

40 Fischer, F. P. Experimentelle Beiträge zum Begriff der Sehrichtungsgemeinschaft der Netzhäute auf Grund der binokularen Noniusmethode, *Arch f d ges Physiol* **204** 234, 1924. Ames, A., Jr., Ogle, K. N., and Gliddon, G. H. Corresponding Retinal Points, the Horopter and Size and Shape of Ocular Images, *J Optic Soc America* **22** 538, 1932. Brecher, G. A. Form und Ausdehnung der Panum'schen Areale bei fovealem Sehen, *Arch f d ges Physiol* **246** 315, 1942.

though the strabismus may have begun in infancy. On the other hand, if the strabismus is purely unilateral and of long standing, the retinal correspondence is almost always anomalous. However, if one forces such a patient to fixate with the usually deviated eye, one may suddenly find that he localizes according to normal correspondence. This can be explained by the fact that anomalous correspondence is established on the basis of the usage of the eyes. If the patient is forced to use his eyes in a way unusual for him, the innate, normal correspondence will at once come into play. The situation is similar in the aforementioned cases of facultative divergent strabismus, in which the patients show a normal sensorial reaction when there is binocular fixation but anomalous correspondence when the eyes are dissociated.

In general, one can state the rule that the more unstable the motor condition is, the less stable is the sensorial reaction. The visual acuity plays no, or only a minor, role, and even a high amblyopia ex anopsia will not prevent the appearance of an anomalous correspondence.

Another factor which has to be considered is the individual difference in adaptability. Not all persons are equally well able to make adjustments, and young persons are generally more adaptable than older ones. This may explain why anomalous correspondence is found more frequently in cases in which the strabismus began early in life.

One must, furthermore, bear in mind that anomalous correspondence is a process which requires time—more time in people with low adaptability, less time in people with high adaptability. It will depend, therefore, largely on the time elapsed since the onset of the strabismus or since a change in the motor condition occurred under the influence of therapeutic measures (glasses, operations, orthoptic exercises) whether normal or anomalous correspondence, or both, will be found.

It must, finally, be reemphasized that the type of sensorial reaction elicited in the examination is also determined by the type of test used and by the way in which it is administered.

The clinical picture of the sensorial retinal relationship in concomitant strabismus is a varied one, the results of the tests in the individual case depend on all the factors which have just been discussed. These factors which influence the establishing of anomalous retinal correspondence and its clinical determination may be summarized as follows: (1) the stage of the development of binocular vision prior to the onset of the strabismus, (2) the type and stability of the motor anomaly (i.e., the use made by the patient of his eyes in ordinary life), (3) the patient's individual adaptability and his age at the time of the onset of the strabismus, (4) the time elapsed since the strabismus became manifest or since therapeutic measures affecting the angle of squint were instituted, and (5) the type of test used and the way in which it was administered.

I shall illustrate now, by means of case histories,⁴¹ some of the types of sensorial retinal relationship as they are met with in the examination of patients with concomitant strabismus

1 NORMAL CORRESPONDENCE IN SPITE OF EARLY ONSET OF STRABISMUS

CASE 3—E G, a white girl aged 14 years, came for examination because of considerable eyestrain in close work and in watching moving pictures. Her family history was negative so far as strabismus or other serious ocular defects were concerned. The patient had never been seriously ill. When she was 1½ years of age, it was first noticed that her left eye turned out occasionally, especially when she was tired. This condition had not changed, except for a possible slight improvement during the past few years. At the age of 3 years she was given a pair of glasses, while she wore these glasses the left eye turned out more frequently. The glasses were discarded when the patient was 7 years of age, she had not worn glasses since, nor had there been any other ocular therapy.

Refraction and Visual Acuity—Right eye +1.75 D sph \subset -0.50 D cyl, axis 20 = 20/15 -1, left eye +2.00 D sph = 20/20 +1

Retinal Correspondence—The patient had binocular fixation for distance, but at the slightest provocation (a short and partial covering) the left eye turned out and up, covering the right eye caused this eye to turn out and slightly upward. The cover test revealed a divergent strabismus of 15 arc degrees, with pronounced and variable dissociated vertical divergence.

Double Image Test There was 15 arc degrees of crossed diplopia with either eye fixating, with 2 to 3 arc degrees of right hypertropia with the red glass in front of the right eye and 8 to 10 arc degrees of left hypertropia with the red glass in front of the left eye (indicating left hypertropia combined with dissociated vertical divergence).

After-Image Test There was normal localization of positive and negative double images. The near point of convergence was at 10 cm, convergence was held poorly. However, the patient was able, most of the time, to fixate binocularly at reading distance.

Bar Reading When fixating binocularly, the patient was able to bar read, when the left eye was in a divergent position, the patient suppressed the images reaching that eye.

Stereoscopic Test Pictures requiring the second degree of fusion were at times fused, at others the images of the left eye were suppressed, with stereoscopic pictures (Keystone chart DB₆) there was always 100 per cent stereopsis.

Synoptophore Objectively and subjectively, there were 25Δ of exophoria and 5Δ of left hypertropia, the eyes were always dissociated when first degree

⁴¹ These cases were selected, more or less at random, from several hundred cases of concomitant strabismus. They were chosen because they were representative of a certain type of sensorial retinal reaction, not because they were unique. For every type, with the exception of one or two, numerous other examples could be quoted. It is my purpose in the present paper to bring out the typical forms rather than to determine their frequency. The latter will be done in a statistical study of strabismus which is in preparation. Unless it is differently stated, the patients did not show any extraocular or intraocular disease or anomaly except for the strabismus.

pictures were used, there was better cooperation with second degree pictures, and with third degree pictures she always fused, with depth perception

This instructive case presents the following features. The patient had a divergent strabismus of the left eye and a marked dissociated vertical divergence, indicating that innervational factors played a large part in causing her condition. She was able to overcome the deviation of the left eye both for distance and for near vision, aided in this undoubtedly by her hyperopia. Thus, the strabismus remained latent most of the time, and there was no reason for the development of an anomalous correspondence, which was not found in any of the tests. In fact, the patient had excellent binocular cooperation as long as she kept her divergent strabismus latent, but she needed a strong fusional stimulus to do so. The prognosis in this case is very good. A surgical correction which would remove the necessity for a constant exertion of the convergence, and orthoptic exercises to improve the fusional conditions, should remove completely the subjective symptoms of eyestrain and allow the patient to wear a correction for her hyperopia.

Cases of this type are met with when the patient has a divergent strabismus which he can correct by a convergence impulse, but not all patients show complete absence of anomalous correspondence or such a high degree of binocular cooperation as the patient in case 3.

CASE 4—K. G., a white girl aged 9 years, had a family history without evidence of ocular disorders. When the child was 2 years of age, it was first noticed that her right eye turned out occasionally, especially when she was tired. This condition had remained unchanged since. At the age of 4 years she had orthoptic exercises, which were carried out for two years but were finally discontinued at the suggestion of the physician, who thought them useless. The patient had had no therapy since that time, she had never worn glasses and had no complaint.

Refraction and Visual Acuity—Right eye = left eye $+1.25$ D sph = 20/20

Retinal Correspondence—Most of the time there was binocular fixation for distance, but the eyes were easily dissociated in the cover test, which showed divergent strabismus, with an angle of squint of 15 to 17 arc degrees.

Double Image Test The double images were easily perceived. Their distance varied considerably during the test, most of the time there was a slightly uncrossed diplopia, but at times the patient showed a crossed diplopia of 16 arc degrees. There was no difference in the localization when the fixation changed from the right eye to the left.

After-Image Test Both the positive and the negative after-images were seen alternately, thus $\begin{array}{c} | R \\ \text{---} \text{---} L \\ | \end{array}$
and thus $L \text{---} \text{---} \left. \begin{array}{c} | \\ | \end{array} \right\} R$, indicating the presence of both normal localization and anomalous localization adapted to the angle of squint.

Stereoscope The patient had fusion and 100 per cent depth perception with the Keystone DB_a chart.

Synoptophore The objective angle was about 25Δ with first degree pictures, it was difficult for the patient to join these pictures, at times she did so at the objective angle, and at others at zero (anomalous correspondence). However, she joined second and third degree pictures with normal correspondence and depth perception at zero, overcoming her strabismus.

Bar Reading She could bar read and converge fairly well on a pencil.

This case is quite similar to case 3 except for one important factor. The child K. G. also had a divergent strabismus, which she was able to overcome by a convergence impulse, and as long as she kept her strabismus latent her eyes cooperated normally. But all three tests used—the synoptophore test, the double image test and the after-image test—disclosed the presence of an anomalous correspondence with the normal correspondence when the eyes were dissociated. This indicates that the patient's eyes were frequently dissociated and that she had, therefore, acquired a sensorial retinal relationship adapted to this dissociated position.

It is of interest to note that in both case 3 and case 4 the strabismus could be kept latent and that the retinal correspondence was normal when strong fusional stimuli, particularly disparate stimuli, were offered. With first degree pictures in the stereoscope and the synoptophore there was dissociation, and in case 4 anomalous correspondence. Similar observations can be made in certain cases of convergent strabismus.

CASE 5—B. P. B., a white girl 6 years of age, had a negative family history for ocular disorders. Soon after the patient's birth the mother noticed a cast in the right eye. The child had been examined by an ophthalmologist every year since then. Glasses had never been prescribed, but for a while drops (atropine?) were used.

Refraction and Visual Acuity—Right eye $+1.50$ D sph = 20/20, left eye $+1.75$ D sph $\times 0.25$ D cyl, axis 85 = 20/30.

Retinal Correspondence—The cover test showed convergent strabismus of 5 arc degrees in the right eye. The after-image test showed normal correspondence. The double image test revealed both normal and anomalous localization of double images.

Synoptoscope With first degree pictures, the objective angle was 10Δ and the subjective angle 2Δ of esophoria, with second degree pictures normal correspondence was obtained.

In this case of low hyperopia with small convergent deviation and slight amblyopia of the left eye the anomalous correspondence was again only superficially established, this is apparent from the fact that the localization of the after-images was always normal and that both normal and anomalous correspondence were evident in the double image test and in the test with the synoptoscope. The feature of the case which I wish particularly to stress is the appearance of normal correspondence when strong fusional stimuli were exerted (second degree pictures in the synoptoscope), while the correspondence was anomalous when there

were no, or only weak, fusional stimuli (first degree pictures in the synoptoscope) This finding, aside from being of prognostic value as to the result of orthoptic exercises, indicated that the patient could and did use her eyes together when the conditions were favorable It must not be construed as being in contradiction to the thesis, set forth in the discussion of the tests for retinal correspondence, that one is more likely to elicit anomalous correspondence the closer the conditions of the test approximate the normal conditions of seeing In this case the eyes were frequently used properly in normal environments Only when the conditions for fusion were poor (either because no fusional stimuli were present in the field of view or because the child was tired) did the eyes dissociate; but this had happened frequently enough to permit the development of anomalous correspondence

The reason that the children in cases, 3, 4 and 5 showed normal correspondence in spite of an early onset of strabismus is to be found in the ability of all 3 patients to keep their eyes straight and use them together a good deal of the time There is a second group of patients who persist in localizing according to the innate normal correspondence, but who do so for exactly the opposite reason These patients retain the normal correspondence because they have never kept their eyes straight and have never used them together, so that there has arisen no opportunity for the development of anomalous correspondence

CASE 6—E R, a white girl, was 8 years old when she was first seen A paternal aunt had strabismus, the family history was otherwise negative for ocular difficulty It was first noticed when the child was 18 months of age that the right eye was turning in, this occurred after a sickness from whooping cough and measles She had worn glasses since the age of 3 years but had had no other treatment

Refraction and Visual Acuity—Right eye $+5.00$ D sph $\subset +1.00$ D cyl, axis $90 = 20/100 - 1$, left eye $+5.00$ D sph $= 20/20$

Retinal Correspondence—In the cover test, with correction there was a convergent strabismus of the right eye of 25 arc degrees, covered to a large extent by a negative angle gamma The double image test and the after-image test showed normal correspondence

A tenotomy of the right internal rectus muscle reduced the angle of squint to 9 arc degrees, owing to the large angle gamma, the eyes appeared parallel for distance Two years later the double image and after-image tests still showed normal correspondence

In this case of high hyperopia, high amblyopia and unilateral strabismus of large amount, one is justified in assuming that the binocular cooperation never developed beyond the stage of innate common visual directions and that the patient never used her eyes together sufficiently to establish anomalous correspondence But a similar behavior can also be observed in cases of alternating strabismus in which the visual acuity is equal in the two eyes and in which the angle of squint—at least with correction—is not very large

CASE 7—B P, a white girl, was 5 years of age when first seen, she had been observed over a period of four years. Her mother was highly far sighted and had intermittent convergent strabismus, several members of the family on the maternal side were highly far sighted. It had been noticed since the patient's birth that either eye turned in intermittently, she had had no previous ocular examination or treatment.

Refraction and Visual Acuity—Right eye +5.00 D. sph \subset +2.00 D. cyl, axis 75 = 20/25, left eye +5.00 D. sph \subset +2.00 D. cyl, axis 90 = 20/25.

Retinal Correspondence—In the cover test there was alternating convergent strabismus of 35 to 40 arc degrees without glasses and of 15 to 16 arc degrees with glasses, with some left hypertropia. Because of a large angle gamma, the eyes appeared straight with glasses. The patient could fixate with either eye and alternated to some extent at will but preferred the right eye for fixation. There was a slight excess of adduction in each eye, being greater in the left eye, with pronounced overfunction of the left inferior oblique muscle.

Synoptophore. The objective angle of squint was 34Δ , with $2\frac{1}{2}\Delta$ of left hypertropia, and a subjective angle of 2 to 4Δ .

Double Image Test. At times there was no horizontal displacement of the double images, at others there was 15 arc degrees of uncrossed diplopia with either eye fixating.

After-Image Test. Positive and negative after-images were always normally localized.

Stereoscopic Examination. There was always strictly unocular vision.

This patient came from a highly hyperopic family on the maternal side. She herself had a typical accommodative strabismus with equal visual acuity of the two eyes. The strabismus, noticeable since her birth, had always been alternating. She had apparently used her eyes together only infrequently, and there was therefore no reason for her to acquire a deeply rooted anomalous correspondence. She showed, accordingly, always a normal localization of the after-images. There was, however, at times an anomalous correspondence adapted to the angle of squint in the synoptophore and in the double image test, which is proof of the existence of occasional cooperation of her two eyes. But this cooperation was not of sufficient duration or frequency to cause a complete repression of the normal retinal relationship.

Cases 6 and 7 are particularly significant in a theoretic respect. They can be interpreted only on the basis of the nativistic theory. If the common visual directions were acquired by proper use of the eyes, then a child who has had a strabismus ever since birth could not show a normal retinal relationship, the commonness of the visual directions must have existed prior to and independent of the use of the eyes, in other words, it is innate.

2 ANOMALOUS CORRESPONDENCE ADAPTED TO THE ANGLE OF SQUINT

CASE 8—J M, a white girl 16 years of age, had one cross-eyed cousin. Otherwise there was no strabismus in the family. When the patient was 2 years of age, an alternating convergent strabismus developed, following whooping cough.

She had worn glasses since the age of 4 years and had had prism fit-overs (both eyes, 6 Δ base out) for one year. She had had no other therapy. Between the ages of 6 to 8 years she had occasional spontaneous diplopia, but never since.

Refraction and Visual Acuity—Right eye +1.75 D sph = 20/20, left eye +1.75 D sph = 20/15

Retinal Correspondence—Cover Test With refractive correction, there was 12 to 15 arc degrees of alternating convergent strabismus for distance and near vision, the left eye was preferred for fixation.

Double Image Test With the refractive correction alone there was an uncrossed diplopia of 6 arc degrees with either eye fixating, with refractive correction and prism fit-overs there was no horizontal displacement of the double images, although the cover test still showed 6 arc degrees of alternating convergent strabismus. *After-Image Test* The after-images were normally localized.

Stereoscope Most of the time there was alternating unocular vision; at times there was fusion of second degree pictures, but there was no stereopsis.

In this case the normal correspondence was no longer as prevalent as in the preceding cases. The patient's response to the after-image test was normal, to be sure, but the double image test showed a well established anomalous correspondence, and the angle of anomaly was, interestingly enough, adapted to the peculiar circumstances of the case. With her refractive correction, the patient had objectively 12 arc degrees of convergent strabismus, and in the double image test, an angle of anomaly of 6 arc degrees. This angle of anomaly corresponded exactly to the residual angle of squint when the prism fit-overs were worn. In other words, the patient had acquired an angle of anomaly which exactly offset the deviation to which she had become accustomed by wearing the prism fit-overs constantly for about one year.

Such an adaptation to the particular circumstances of the case is often well demonstrated in cases of accommodative strabismus when the patient's sensorial reaction is tested with and without his glasses.

CASE 9—M. S., a white boy, "was 3 years of age when first seen. Both his father and his mother had an amblyopic eye. One year prior to the examination the boy had whooping cough, after which an occasional turning of the left eye was observed. The patient had not been treated previously for his ocular condition.

Refraction and Visual Acuity—Right eye +5.00 D sph = 20/20—, left eye +5.00 D sph = 20/70

Retinal Correspondence—The patient wore these glasses constantly for three years. At the end of this period the following condition was found. Cover test Without correction there was 22 arc degrees of convergent strabismus in the left eye, with correction the angle of squint was reduced to 10 arc degrees.

Double Image Test With correction double images coincided, without correction there was an uncrossed diplopia of 10 arc degrees.

After-Image Test Positive and negative after-images showed a horizontal separation of 10 arc degrees, irrespective of whether or not glasses were worn.

Synoptophore Objectively, there was 10 arc degrees of esotropia with correction and 24 arc degrees without correction. Subjectively, with correction the angle was zero, and without correction there was 12 arc degrees of esotropia with first degree pictures.

The retinal correspondence in this case was harmoniously adapted to the angle of squint existing when the patient wore his correction. When the retinal correspondence was tested with the synoptophore and in the double image test, a harmonious anomalous correspondence was found when the patient wore his glasses, the anomalous retinal correspondence was unharmonious in these tests when the patient did not have his glasses on. The result of the after-image test was, of course, not influenced by the glasses.

In this case the retinal correspondence was fully adapted to the patient's habitual angle of squint. The situation was similar in the next case.

CASE 10—A MacD, a white girl 9 years old, had a negative family history for ocular disorders. It had been noticed since she was born that her right eye turned in. She had worn glasses since the age of 4 years but otherwise had had no therapy.

Refraction and Visual Acuity—Right eye +3.00 D sph \subset +0.50 D cyl, axis 90 = 20/30—2, left eye +3.00 D sph +0.50 D cyl, axis 90 = 20/20.

Retinal Correspondence—Cover Test. There were 6 arc degrees of convergent strabismus in the right eye.

Double Image Test. The double images coincided and followed the prism displacement in all directions.

After-Image Test. The positive and negative after-images were seen thus

$$\begin{array}{c} |R \\ \hline | \end{array} \quad \text{---} \quad L$$

The interpretation of this case is simple. The patient had a unilateral convergent strabismus of long standing and small amount. For a number of years she had worn an adequate correction for her hyperopia. Her neuromuscular condition had been balanced for a number of years, and she had acquired a well established anomalous correspondence, both the double and the after-image test showed a localization adapted to the angle of squint.

The fact that such cases exist and are, indeed, rather frequent is one of the most important arguments in favor of the concept of anomalous correspondence adopted in this paper.

If this concept is correct, there ought to be an adaptation of the visual directions not only in the horizontal but also in the vertical sense. Such an occurrence can occasionally be observed, particularly if the vertical deviation is large.

CASE 11—M W R, a white youth aged 18, a high school student, had a maternal uncle who was cross eyed. The patient himself had been cross eyed since the age of 2½ years, when he fell downstairs, after which his right arm was paralyzed for a while.

Refraction and Visual Acuity—Right eye +3.00 D sph \subset -2.50 D cyl, axis 10 = 20/20, left eye +3.00 D sph \subset -3.00 D cyl, axis 170 = 20/20.

Retinal Correspondence—The patient fixated most of the time with the right eye but was able to alternate the fixating eye at will. There was an alternating

convergent strabismus of approximately 40 arc degrees, with approximately 6 arc degrees of left hypertropia and a dissociated vertical divergence. The adduction was extremely excessive, particularly in the right eye. The abduction was deficient. The case was complicated by other deficiencies and overactions in the excursions of the eyeballs which are not pertinent to the present discussion.

Double Image Test There was either no horizontal deviation or an uncrossed diplopia of 10 to 14 arc degrees when fixating with either eye, a dissociated vertical divergence of up to 3 or 4 arc degrees became manifest after covering either eye for a few seconds with the red glass.

After-Image Test The horizontal after-image (both positive and negative) was separated by a very large distance from the vertical after-image (35 to 40 arc degrees) and was higher when produced in the left eye and lower when produced in the right eye (vertical distance approximately 6 arc degrees). The patient was operated on, with good cosmetic result in so far as the horizontal deviation was concerned. The after-image test, taken at frequent intervals, had yielded the same result over a period of nearly two years.

In this patient, a sensorial adaptation to the motor condition had taken place not only in the horizontal but also in the vertical direction. In the double image test there was no vertical displacement of the double images (except for the concurrent dissociated vertical divergence), and in the after-image test there was a vertical separation of the after-images, which corresponded to the patient's left hypertropia.

However, as was pointed out, the adaptation of the sensorial retinal relationship to changed mechanical conditions is a process requiring time. It would not be reasonable to expect it to be accomplished at all levels at the same time. One therefore finds quite often that the angle of anomaly is not adapted to the angle of squint, either in one or in all of the tests. There is always a reason for this (for instance, a recent operation which has changed the position of the eyes), which may or may not be known.

3 ANOMALOUS CORRESPONDENCE PARTIALLY ADAPTED TO THE ANGLE OF SQUINT

CASE 12—G. H., a 13 year old girl, was the daughter of irresponsible parents and was herself of a mental age considerably below her chronologic age. No ocular history was available. The child complained of eyestrain.

Refraction and Visual Acuity—Right eye $+2.00$ D sph = 20/20, left eye $+2.50$ D sph = 20/70.

Retinal Correspondence—**Cover Test** The left eye showed convergent strabismus of 5 to 6 arc degrees. The patient was able to fixate with the left eye.

Double Image Test Repeated tests showed that the double images coincided and followed exactly the prism displacement in all directions.

After-Image Test The negative after-images were seen thus (a positive after-image could not be obtained) R — — — — — | L

This case is reported because of the difference in the results of the double image and the after-image test. In the double image test the

angle of anomaly was 5 to 6 arc degrees, in the after-image test, 15 to 16 arc degrees. This can be interpreted only as meaning that the angle of squint had been larger at some time before than it was at the time of the examination, and that the sensorial condition was not as yet fully adapted to the changed motor conditions. Such an adaptation had taken place as far as the ordinary conditions of seeing were concerned, which were approximated in the double image test. But as soon as the patient was given an unusual visual problem, such as is provided in the after-image test, a former mode of localization was resorted to.

It is not known why the angle of squint had changed in this case, but in other cases it is known that the change was caused by an operative procedure. The history of a case belonging to this group is reported next.

CASE 13—A M, an Italian aged 43, came for examination because he felt the need of a change in his glasses. The family history was negative for strabismus. The patient's right eye began to turn in when he was 2 years of age, after a severe infectious disease, possibly encephalitis. At the age of 27 he was operated on for his strabismus.

Refraction and Visual Acuity—Right eye +4.00 D sph \subset +1.00 D cyl, axis 90 = 20/400, left eye +3.00 D sph \subset +1.25 D cyl, axis 90 = 20/20.

Retinal Correspondence—For distance there was a convergent strabismus of the right eye, the movement was offset in the cover test by a prism of 15 Δ . The rotations of both eyes were normal. The double image test showed uncrossed diplopia of 2 arc degrees when the left eye fixated and crossed diplopia of 2 arc degrees when the right eye fixated. In the after-image test, the positive and

R
|
negative after-images were seen thus — — — L
|

It is quite apparent that in this case of high hyperopic astigmatism and amblyopia ex anopsia of the right eye the double image test was roughly adapted to the present small angle of squint, while the after-image test showed an anomalous relationship adapted to the pre-operative angle of about 30 to 35 arc degrees. It is of interest to note that this anomalous relationship still existed, although the operative change in the position of the eyes had occurred sixteen years prior to the examination.

That the interpretation given to the findings in this case is correct is shown by a case which I have followed over a period of six years.

CASE 14—M W, a white school girl, was 16 years of age when first seen. She had a negative family history for ocular disease. Her left eye had turned in since birth. She had worn glasses since the age of 6 years, for a time the right eye was occluded.

Refraction and Visual Acuity—Right eye +1.00 D sph \subset +2.25 D cyl, axis 75 = 20/20, left eye +1.00 D sph \subset +2.25 D cyl, axis 105 = 20/25—2.

Retinal Correspondence—The cover test showed convergent strabismus of the left eye of 20 arc degrees. There was an excess of adduction, particularly in

the left eye, an overfunction of the inferior oblique muscles, and a pronounced dissociated vertical divergence. The double image test showed anomalous correspondence adapted to the angle of squint. The positive and negative after-images

were seen thus R — — — — — | L
|

A tenotomy of the left internal rectus was performed, which reduced the angle of squint to 8 or 10 arc degrees. After the operation the double image test showed crossed diplopia of 8 arc degrees, the after-image test showed no change. Two years after the operation the localization of the double images was adapted to the angle of squint, the after-images were still localized in the same way as before the operation. Six years after the operation, when the patient was seen last, refraction and visual acuity were essentially unchanged. The cover test showed a residue of convergence of 8 arc degrees, covered by a large angle gamma. There was a deficiency of adduction in the right eye, the condition of the motility was otherwise unchanged. The double image test showed at times only vertical displacement of double images according to the vertical divergence and at others 2 arc degrees of uncrossed diplopia. The localization of the after-images was the same as before the operation.

The history of this patient demonstrates that in cases of deeply rooted anomalous correspondence the after-images may be localized in an anomalous way adapted to the preoperative angle of squint even many years after the operation. Only a partial adaptation to the postoperative mechanical conditions had taken place in this case, as was evidenced by the double image test, but the adaptation was too superficial to have caused a change in the localization of the after-images. This explains the difference between the results of the double image and the after-image test.

4 CHANGE IN SENSORIAL REACTION WITH DISSOCIATION OF THE EYES

In cases 4 and 5, in which both normal and anomalous correspondence were present, a careful observation of the patient's eyes during the tests showed that the change in localization was not accomplished by a change in the position of the patient's eyes. In certain rare instances, however, it can be demonstrated even in the after-image test that the position of the patient's eyes (i. e., whether or not the eyes are dissociated) influences the type of localization used by the patient. The results obtained in these cases, which were mentioned in the discussion of the after-image test, might easily be misconstrued, and I therefore cite an instructive case belonging to this group.

CASE 15—F. P. C., a white man aged 32, with a negative family history for ocular disorders, complained of photophobia, ocular fatigue and severe headaches after using his eyes. It had been noticed since he was 3 years of age that either eye turned out, and ever since he could remember he had had the ability to let either eye turn out at will. The patient had always had good health, but he claimed to be highly nervous, in fact, a few years previous to the examination he had a severe nervous breakdown and had to be confined to an institution.

Refraction and Visual Acuity—Right eye = left eye + 0.25 cyl, axis 90 = 20/15

Retinal Correspondence—The eyes were parallel for distance, but the cover test showed an alternating divergent strabismus of 25 arc degrees. The patient could control his eyes perfectly, he could either keep them straight or let either eye diverge at will. He converged perfectly on a pencil, and the convergence was well held. In the double image test, when the red glass was placed in front of either eye for a very short while, the double images coincided, but when the red glass was kept long enough in front of one eye so that the eyes were dissociated, the localization of the double images became extremely uncertain. The patient reported most of the time that he saw two entirely separate images which had no relation to each other, although he saw them simultaneously. This behavior was checked with the projection instrument, in which the two eyes are dissociated by means of polaroid material.¹⁴ When a dot was presented to one eye and a tangent scale to the other eye, the patient was again unable to localize the dot in relation to the scale, but when a binocularly seen square of light was projected at the same time on the screen, the patient fused the square and localized the dot properly in relation to the tangent scale. The results obtained with the after-image test were particularly interesting. The positive after-images were always localized according to anomalous correspondence adapted to the angle

of squint

$$\begin{array}{c} L | \\ | \\ \text{of squint} \end{array} \quad \begin{array}{c} \text{---} \quad \text{---} \\ | \end{array} \quad R$$

The negative after-images were localized either

thus

$$\begin{array}{c} L | \\ | \end{array} \quad \begin{array}{c} \text{---} \quad \text{---} \\ | \end{array} \quad R \quad \text{or thus} \quad \begin{array}{c} | L \\ | \end{array} \quad \begin{array}{c} \text{---} \quad \text{---} \\ | \end{array} \quad R$$

The first mode of localization occurred when the patient dissociated his eyes, the second, when he kept them straight (which he could do in the lighted room, but not in the dark). With the stereoscope, as well as for distance with the projection instrument, the patient had 100 per cent depth perception with the DB₆ Keystone chart.

There was a pronounced deficiency of adduction in both eyes, and advancement with resection of both internal rectus muscles was performed. One month after the operation, there was a residue of divergence of 5 arc degrees in the cover test, the patient was no longer able to dissociate his eyes at will. In the double image test there was an uncrossed diplopia of 20 to 22 arc degrees (anomalous correspondence adapted to the preoperative angle of squint), and there was now no difficulty in localizing the double images. As before the operation, the double images coincided when the red glass was placed only for a short while in front of one eye. The positive after-images were now localized most of the time normally, occasionally there was a displacement of the vertical after-image of the same amount as prior to the operation. The negative after-images always formed a cross, in none of the numerous tests were they localized anomalously.

The salient features of this highly interesting case can be summarized as follows. The patient had a facultative divergent strabismus of 25 arc degrees. When he kept his eyes straight, he had normal binocular vision. When his eyes were dissociated, he showed anomalous correspondence in the double image test. Before he was operated on, he had great difficulty in localizing the double images, but it can be assumed that his anomalous sensorial reaction in this test was adapted to the angle

of squint, since he showed a crossed diplopia of 20 arc degrees after the operation, which had reduced his angle of divergent strabismus from 25 to 5 arc degrees. After the operation he had no difficulty in localizing the double images. The after-image test showed a peculiar behavior. The positive after-images (seen by the patient in the dark) always presented a displacement adapted to the angle of squint, the negative after-images either formed a cross or were displaced by the amount of the angle of squint, according to whether or not the eyes were dissociated. The fact that the patient was unable to keep his eyes straight in the completely darkened room explains why the positive after-images never appeared as a cross. After the operation the behavior of the after-images changed to some extent. The patient was now unable to dissociate his eyes at will, and the negative after-images were always localized normally. This mode of localization prevailed even in the dark, only occasionally was there a recurrence of the old mode of localization.

It must be emphasized once more that even in this case the position of the after-images did not change because of the change in the direction of the line of gaze of one eye when the eyes were dissociated. The change in the position of the after-images was caused by a change in the sensorial retinal relationship, which in this particular instance was dependent on whether or not the eyes were used together.

The difference in the localization of the positive and the negative after-images shown by this patient is typical for cases with facultative divergent strabismus. A number of instances could be cited to corroborate this statement, but I shall restrict myself to referring to a case history which I have recently published.⁴²

If the explanation given here for the phenomenon is correct, the phenomenon should not occur in patients who are unable to control the position of their eyes. I do not recall any instance in which it did. However, at times even such patients show differences in the localization of the after-images, as will be seen in the next case.

CASE 16—T. M. C., a white girl aged 9 years, had a negative family history for strabismus. Only when she was 4 years of age, after a fall downstairs, was it noticed that her left eye began to turn in.

Refraction and Visual Acuity—Right eye +5.00 D sph \subset +0.50 D cyl, axis 90 = 20/20, left eye +4.00 D sph \subset +2.50 D cyl, axis 110 = 20/40 + 3.

Correspondence—With this correction there was a convergent strabismus of the left eye of 20 arc degrees. The patient fixated habitually with the right eye but was able to fixate with the left eye.

Double Image Test—Most of the time there was 20 arc degrees of uncrossed diplopia with either eye fixating, occasionally there was no horizontal deviation of the double images, but this occurred only when the right eye fixated.

⁴² Burian, H. M. A Visual Phenomenon Related to Binocular Triplopia, *Am J Ophth* 26:1084, 1943.

After-Image Test The positive after-images were always localized according to normal correspondence, the negative ones were localized almost always according to anomalous correspondence adapted to the angle of squint.

The behavior of this patient in the after-image test was the reverse of the behavior shown by patients with facultative divergent strabismus. In the darkened room there was normal correspondence, in the lighted room the correspondence was anomalous. The reason for this is that the conditions of seeing in the darkened room were unusual for the patient. Her anomalous correspondence was not deeply rooted, as was evidenced also by the double image test, and she reverted immediately to the normal mode of localization when placed under an unusual condition.

There is no contradiction in the response of the after-image test in the two types of cases discussed in this section. In fact, the findings supplement and corroborate each other.

5 CHANGE IN SENSORIAL REACTION WITH CHANGE IN FIXATION AND WITH SELECTIVE STIMULATION OF VARIOUS RETINAL AREAS

Changes in the sensorial reaction occur not only depending on whether or not the eyes of the patient are dissociated, they may also occur when fixation is changed from one eye to the other⁴³. This difference in reaction is, again, not due to the change in the actual position of the eyes.

CASE 17—J C W was a white girl aged 7 years whose father had strabismus. It was noticed when she was $2\frac{1}{2}$ years of age that her left eye turned in, the convergence being greater when she was tired. She had worn glasses for some time but had had no other therapy.

Refraction and Visual Acuity—Right eye +1.50 D sph \subset +1.50 D cyl, axis 70 = 20/20, left eye +0.75 D sph \subset +2.75 D cyl, axis 90 = 20/30.

Retinal Correspondence—Cover Test. There was 8 arc degrees of convergent strabismus of the left eye.

Double Image Test When the right eye fixated, the double images were slightly crossed or slightly uncrossed (anomalous correspondence), when the left eye fixated, there was an uncrossed diplopia of 8 arc degrees (normal correspondence).

After-Image Test The after-images were localized according to normal correspondence.

This patient had normal correspondence in the after-image test. In the double image test she showed anomalous correspondence when she fixated with her right eye. But when she was forced to fixate with

⁴³ The first to observe such behavior was A. von Graefe, in 1855¹⁹. His patient showed a small residue of convergent strabismus of the left eye after operation. When the patient fixated with the right eye, there was always a crossed diplopia with considerable distance of the double images (anomalous correspondence). When he fixated with the usually deviated left eye, there was an uncrossed diplopia of small amount (normal correspondence).

her left eye, which was usually deviated, she used her eyes under conditions to which she was not accustomed and she localized immediately in the normal way. In this patient the anomalous correspondence was not deeply rooted, but the same behavior can be observed in patients in whom the anomalous correspondence has gained a much stronger hold.

CASE 18—J. B., a white girl aged 12, had been under my observation since she was $6\frac{1}{2}$ years of age. She had a maternal uncle with strabismus, turning of her right eye was first noticed when she was 4 years of age.

Refraction and Visual Acuity—Right eye $+3.00$ D sph $\subset +2.00$ D cyl, axis $90 = 20/20 + 1$, left eye $+2.75$ D sph $\subset +1.00$ D cyl, axis $100 = 20/20$.

Retinal Correspondence—Cover Test. There was 5 to 6 arc degrees of convergent strabismus of the right eye.

Double Image Test. There were crossed diplopia of 8 to 10 arc degrees when the left eye fixated (anomalous correspondence) and uncrossed diplopia of 5 arc degrees when the right eye fixated (normal correspondence).

After-Image Test. Positive and negative after-images showed anomalous correspondence angle of anomaly 15 arc degrees)

$$\begin{array}{c} | R \\ \text{---} \text{---} L \\ | \end{array}$$

On two occasions the positive after-images were localized thus

$$\begin{array}{c} | R \\ \text{---} \text{---} L \text{ (angle of anomaly 5 to 6 arc degrees)} \\ | \end{array}$$

Synoptophore. There was an objective angle of 10 to 12Δ of esophoria and a subjective angle of zero.

In this case there was, again, a difference in the mode of localization of the double images, depending on whether the patient fixated with the habitually deviated eye or with the eye that habitually fixated. Again, the correspondence was normal when the patient fixated with the eye which was as a rule turned.

The case is especially interesting because the patient presented two types of anomalous localization. In the synoptophore test the angle of anomaly was equal to the angle of squint, in other words, in this test, which most closely approximates the habitual conditions of seeing, the anomalous correspondence was adapted to the anomalous motor condition revealed by the cover test. In the double image test as well as in the after-image test, the angle of anomaly was larger than the angle of squint, indicating again that the angle of squint must have been larger in times past. One encounters such a situation relatively frequently in the after-image test, but it is unusual to find it also in the double image test, except shortly after an operation.

A change in the mode of localization takes place not only when the leading eye gives up fixation and the deviated eye assumes it, but also when certain artificial conditions of binocular stimulation are created which differ from those to which the eyes of a squinting patient are habitually exposed.

When a squinting patient fixates a certain object, say, the light of the Maddox cross, the image of that object falls on the fovea of the fixating eye and on an eccentric element of the retina of the other eye. The patient may then show an anomalous localization of the double images. If the arrangements of the test are now changed in such a way that the image of the object is formed on the fovea in both eyes, unusual conditions of bifoveal stimulation are created for which the patient is not adapted. It may then happen, and I have observed this frequently, that the patient suddenly localizes the double images according to normal correspondence. I have described such cases in an earlier publication,¹⁵ and I mention them here in further support of the thesis that in many cases in which the anomalous correspondence is not too deeply rooted it depends on the conditions under which the tests are performed whether a normal or an anomalous sensorial response of the patient will be elicited.

6 POSTOPERATIVE CHANGES IN THE MODE OF SENSORIAL REACTION

The spontaneous changes in the sensorial relationship following an operative change in the position of the eyes offer an excellent means of studying the adaptation of the sensorial reaction to the changed motor conditions.

Both Bielschowsky³¹ and, particularly, Ohm⁴⁴ have paid attention to the postoperative development of the retinal correspondence and have stated that squinting patients go through three stages after successful surgical treatment. In the first stage the correspondence is anomalous, in the second there is a rivalry between normal and anomalous correspondence and in the third the normal correspondence is reestablished.

A development such as that postulated by Ohm would, indeed, seem to be the natural course which one would expect squinting patients to follow whose eyes had been straightened by a surgical procedure. Actually, however, as Ohm himself pointed out, only few patients go through all three stages. The spontaneous development toward normalcy may stop at any stage. The factors on which this development depends are similar to those which influence the preoperative establishment of anomalous correspondence. These factors are (1) the age of the patient at the time of the operation, (2) his individual adaptability, (3) the thoroughness with which the anomalous correspondence was established at the time of the operation, and (4) the use the patient makes of his eyes after the operation.

⁴⁴ Ohm, J. Klinische Untersuchungen über das Verhalten der anomalen Sehrichtungsgemeinschaft der Netzhäute nach der Schieloperation, *Arch f Ophth* 57 439, 1908.

After operation, in rare instances the patient spontaneously regains not only normal correspondence but also normal binocular vision. Much more frequently one finds that either the normal sensorial reaction is now the rule (but that normal binocular vision has not developed) or normal and anomalous localization are alternately present. The majority of the patients do not even reach this second stage of Ohm's spontaneously, but the reaction stabilizes itself in an anomalous sensorial relationship adapted to the new motor conditions, or the patients may even retain, at least in the after-image test, the anomalous correspondence acquired previous to the operation.

Two cases of the latter type have already been discussed (cases 13 and 14). In both instances the patients were relatively old at the time of the operation (16 and 27 years, respectively). They adapted themselves in a superficial way to the new motor conditions created by the operation (anomalous correspondence adapted to the angle of squint in the double image test), but their deeply rooted anomalous correspondence acquired prior to the operation still manifested itself in the after-image test years after the surgical procedure was performed.

The behavior of a small child whom I had under my care was very different in this respect.

CASE 19—M M, a white girl, was $3\frac{1}{2}$ years old when first seen. She had a negative family history for strabismus. It was first noticed one year previous to the examination that the left eye turned in, after the child had had an abscess of the left ear. She received glasses at that time.

Refraction and Visual Acuity—Right eye $+5.00$ D sph = 20/20, left eye $+5.00$ D sph $\subset +0.50$ D cyl, axis 90 = 20/20—2

Retinal Correspondence—The cover test showed 20 to 25 arc degrees of convergence in the left eye. There was a marked excess of adduction in both eyes, with some overaction of the right inferior oblique muscle. The double image test showed no horizontal displacement of the double images and 1 to 2 arc degrees of right hypertropia, the double images followed the prism displacement in all directions. The after-image test was attempted but the result was uncertain. Two years later the condition was unchanged in all respects. A tenotomy of the left internal rectus was performed. The left eye was covered for only two days. Seven days after the operation there was a residue of convergence of 15 arc degrees. Even at that time the double image test again showed no horizontal, but only a vertical, displacement of the double images. Two months after the operation, the residue of convergence was 7 arc degrees, the double image test showed no horizontal displacement and the after-image test presented an anomalous correspondence adapted to the angle of squint (positive

| L
and negative after-images) R — — —
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It is possible that the rapid adaptation of the sensorial to the motor conditions in this case was due to the youth of the patient. It is not accidental, I have seen it happen in a number of instances.

In the second postoperative stage there exists a rivalry between normal and anomalous localization. The normal correspondence is reawakened, but the anomalous correspondence is still present. As a result, two directional localizations were alternately attributed to the foveal stimulations. As a rule, these two directional localizations are present only successively. The foveal stimulus is localized now in a normal, now in an anomalous, way. In certain cases, however, the normal and anomalous localizations are present simultaneously, and the stimulus is then localized in two different directions at the same time. This striking feature is known as monocular diplopia, or binocular triplopia. It is not frequently met with and can often be demonstrated only for a fleeting moment. In other cases it is present more or less constantly and can be observed in the same patient over a number of years.

CASE 20—B. B., a 13 year old white girl, had one cross-eyed cousin. When the patient was 9 months of age, it was first noticed that her left eye was turning in. She had worn glasses for about seven years.

Refraction and Visual Acuity—Right eye $+0.25$ D sph $\subset +0.50$ D cyl, axis $90=20/15$, left eye $+3.00$ D sph $\subset -0.50$ D cyl, axis $55=20/20$.

Correspondence—The cover test showed 20 to 25 arc degrees of convergent strabismus. The patient was able to fixate with the left eye but fixated habitually with the right eye. There was a very large excess of adduction in each eye, a slight overaction of the inferior oblique muscle of the left eye and a dissociated vertical divergence. The results of the double image test were not recorded at the first examination. The after-image test showed anomalous correspondence. A guarded tenotomy of the left internal rectus muscle was performed, the bandage was removed on the second day. On the fourth postoperative day, before being discharged, the patient showed a residue of convergence of 8 to 10 arc degrees in the cover test. The double image test revealed both crossed diplopia of 12 to 14 arc degrees and uncrossed diplopia of 4 to 5 arc degrees, present most of the time successively, and at times binocular triplopia. One month after the operation the angle of squint was again 15 arc degrees. The double image test showed an uncrossed diplopia of about 15 arc degrees with the left eye fixating. With fixation of the right eye localization of the double images was uncertain, but there was always crossed diplopia of about 3 to 4 arc degrees. A guarded tenotomy of the right internal rectus muscle was done, which reduced the angle of squint to 5 arc degrees. On the fourth postoperative day, the double image test showed alternately 20 arc degrees of crossed and 5 arc degrees of uncrossed diplopia, these two types of localization were present either alternately or simultaneously (binocular triplopia). In a later examination the binocular triplopia was never again observed, although the rivalry between normal and anomalous localization continued to exist. Six months after the first tenotomy a myectomy of the left inferior oblique muscle was performed, which completely removed the overaction of that muscle. At that time the crossed and uncrossed diplopia were still both present in the double image test and the after-image test showed both normal and anomalous correspondence. In the course of time the localization of the double images in the double image test tended to become adapted to the angle of squint, the after-image test always showed normal

correspondence The patient was last seen two and a half years after the first operation She then showed 1 arc degree of crossed diplopia when fixating with the right eye and 2 arc degrees of uncrossed diplopia when fixating with the left eye

In some exceptional cases the patient regains spontaneously full binocular vision after an operative correction of the position of his eyes, in spite of an early onset of the strabismus and the existence of anomalous correspondence prior to the operation The following case illustrates this all too rare type At the same time, it offers an example of the cases in which all three stages postulated by Ohm⁴⁴ are successively represented

CASE 21—F S L, a 10 year old white boy with a negative family history for ocular disorders, had had a convergent strabismus since the age of 3 years, after a fall downstairs He had worn glasses since the age of 5 years

Refraction and Visual Acuity—Right eye $+2.75$ D sph = 20/15, left eye $+2.50$ D sph = 20/15

Retinal Correspondence—The cover test showed an alternating convergent strabismus of 24 arc degrees, but the left eye was habitually used for fixation. There were a high bilateral excess of adduction and an overaction of the right inferior oblique muscle The double image test showed anomalous correspondence adapted to the angle of squint, the after-image test revealed both normal and anomalous correspondence Guarded tenotomies of the right and left internal rectus muscles, performed within one month, reduced the angle of squint to 2 arc degrees For a short time after the operations there was crossed diplopia in the double image test, which soon disappeared Five months after the operation there was no movement in the cover test, the double image test showed $\frac{1}{2}$ to 1 arc degree of uncrossed diplopia, and the after-image test was normal In the stereoscope there was alternating unocular vision Eight months after the operation the results of the cover test, the double image test and the after-image test were unchanged, but in the stereoscope there were fusion and 100 per cent depth perception with the graduated Keystone DB₆ and the Bausch and Lomb cards However, the bar reading test indicated absence of binocular vision The condition was the same when the patient was last seen, thirteen months after the operation

7 BINOCULAR COOPERATION IN ANOMALOUS CORRESPONDENCE

If anomalous correspondence is an attempt to restore binocular vision on the basis of an abnormal motor condition, then the question must be asked How successful is this attempt? In other words, is there a binocular visual act in patients with concomitant strabismus and anomalous correspondence comparable to that of normal persons?

The answer is There can be, indeed, a high degree of binocular cooperation with anomalous correspondence It has been shown by other investigators, and in many of the sample cases reported in this paper, that the anomalous correspondence is frequently well adapted to the angle of squint Thus, the basic prerequisite for binocular vision, the commonness of the visual directions of simultaneously stimulated

retinal elements, is fulfilled. There is undoubtedly simultaneous perception with anomalous correspondence, and Bielschowsky^{31a} has demonstrated that binocular color mixture may exist in such cases. I was able to prove that there may even be fusional movements with anomalous corresponding retinal areas,¹⁵ but the highest degree of binocular cooperation, stereopsis, is never achieved.

Again, it must be kept in mind, in studying the binocular visual act in anomalous correspondence, that anomalous retinal correspondence may be more or less well established. If it is present only occasionally and under special conditions, it cannot be expected to afford as complete a binocular cooperation as when it is deeply rooted and established more or less permanently. In the latter condition, however, it may lead to a surprisingly high cooperation between the two eyes. This can be seen from the following case, which concludes this survey of the clinical picture of anomalous correspondence.

CASE 22—M. H., a white girl aged 9 years, had a negative family history for strabismus. Alternate turning in of the eyes was first noticed when the patient was 2 years old.

Refraction and Visual Acuity—Right eye +6.00 D sph \ominus -1.00 D cyl, axis 180 = 20/20, left eye +7.00 D sph \ominus -2.00 D cyl, axis 180 = 20/20 -2.

Correspondence—The patient was observed over a period of four years, and the behavior of her eyes always remained the same. With correction there was an alternating convergent strabismus of 10 arc degrees. The double image test and the after-image test showed anomalous correspondence adapted to the angle of squint. The eyes responded to vertical disparity introduced by prisms (fusional movements present with central stimulation). In the stereoscope there was superimposition of images but alternate suppression of disparate stimuli (grade II binocular vision, no stereopsis). With the projection instrument¹⁵ fusional movements could be elicited when the targets were superimposed on the screen (anomalous correspondence). When the targets were separated according to the angle of squint, a constant rivalry between normal and anomalous correspondence impeded the performance of the test. Stereoscopic targets superimposed on the screen were seen singly, fusional movements occurred when targets were converged up to 10 arc degrees or diverged up to 5 and 6 arc degrees, but, again, there was no stereopsis, there was an alternate suppression of the disparate elements.

IV PRINCIPLES OF TREATMENT OF ANOMALOUS CORRESPONDENCE

The anomalous sensorial retinal relationship is a condition produced by the simultaneous stimulation of the two retinas when the eyes have an abnormal relative position. On the basis of this definition, one can logically divide the methods which might be expected to restore the normal retinal relationship into four groups: (1) methods excluding one eye from the act of vision (occlusion), (2) methods restoring the normal relative position of the eyes (operations), (3) methods pro-

ducing bifoveal stimulation by optical means (prisms), (4) methods employing the simultaneous stimulation of selected retinal areas (orthoptic exercises)

1 METHODS EXCLUDING ONE EYE FROM THE ACT OF VISION (OCCLUSION)

If one eye is permanently excluded from the act of vision by occlusion for a prolonged period, there is no binocular stimulation, and one of the main factors maintaining anomalous correspondence is avoided. I have not made a systematic study of this subject, and my experience is restricted. I am, therefore, unable to state with certainty whether or not occlusion is of definite help in breaking down the anomalous correspondence. However, I do not question that it is frequently a valuable therapeutic adjunct. I have seen a number of cases in which occlusion of the leading eye, instituted for the purpose of improving the vision of the deviated eye, has led in a relatively short time to a notable improvement in the condition of the sensorial retinal relationship. Similar observations were made by Hoorens⁴⁵. Chavasse⁴⁶ claimed that this method may be expected to accomplish more than any method of intermittent stimulation, and Pugh⁴⁷ stated the belief that preoperative and postoperative occlusion were absolutely essential in the treatment of anomalous correspondence.

As an illustration, I am reporting a case which clearly demonstrates the beneficial influence of occlusion.

CASE 23—E. L. T., a white girl 8 years of age, came from a highly hyperopic family on the maternal side. It was noticed that her right eye turned in when she was 2 years of age, she had worn glasses since the age of 4 years.

Refraction and Visual Acuity—Right eye +6.00 D sph \ominus +1.75 D cyl, axis 90 = 20/100, left eye +5.50 D sph \ominus +1.00 D cyl, axis 90 = 20/20.

Retinal Correspondence—The cover test revealed 12 arc degrees of convergent strabismus of the right eye. In the double image test, the double images coincided and followed prism displacement in all directions. In the after-image test, the positive and negative after-images were seen thus, indicating anomalous cor-

respondence adapted to the angle of squint $\begin{array}{c} | \text{R} \\ \text{---} \text{---} \text{L} \\ | \end{array}$

After she had worn an occluder on the left eye for one month, the visual acuity of the right eye improved to 20/70—2, there was no change in the angle of squint or in the localization of the after-images. In the double image test there was now an uncrossed diplopia of 4 arc degrees with either eye fixating. After two more months of wearing the occluder, vision in the right eye had improved to

⁴⁵ Hoorens. Strabismes Concomitants, Bull. Soc. belge d'opht., 1939, no. 78, p. 10.

⁴⁶ Chavasse, F. B. Tests for Secondary Correspondence in Squint, Tr. Ophth. Soc. U. Kingdom 55:482, 1935.

⁴⁷ Pugh, M. A. Squint Training, London, Oxford University Press, 1936.

20/50, the angle of squint still showed 12 arc degrees of convergence, in the double image test there was an uncrossed diplopia of 4 arc degrees, but the after-image test now showed normal localization of the after-images. Occlusion was continued again for two months, after that vision in the right eye had improved to 20/40, in the cover test the localization of both the double images and the after-images was normal. The patient was instructed to leave the occluder off and to return in two months, but she did not return for one year and nine months. When she was seen again, vision in the right eye had regressed to 20/200, the angle of squint was 6 arc degrees of convergent strabismus in the right eye. In the double image test, with the right eye fixating there was 6 arc degrees of uncrossed diplopia, with the left eye fixating there was no horizontal displacement. In the after-image test the positive and negative after-images were

localized as shown in the diagram

$$\begin{array}{c} R \mid \\ \hline \mid \\ \hline L \end{array}$$

She wore again an occluder over the left eye, and after three months she had a corrected vision of 20/50 — 2 in the right eye, the localization of both the after-images and the double images was normal. With continued occlusion for five months longer vision in the right eye improved to 20/30 + 2, the retinal correspondence remained normal.

I believe this case to be of particular interest to the theory of anomalous correspondence. It demonstrates that anomalous correspondence can in suitable cases be broken down by occlusion, as proved in this case by the experiment which the patient unwittingly performed by leaving the occluder off for nearly two years and permitting a relapse into anomalous correspondence. But the case also demonstrates how accurately some highly adaptable persons adjust their sensorial retinal relationship to the existing neuromuscular conditions. When the patient was first seen, she had an angle of squint of 12 arc degrees, later the angle of squint was 6 arc degrees, in both instances she was sensorially fully adapted to the angle of squint. After she had left the occluder off, the only suggestion of the period of reawakened normal correspondence, produced by occlusion, with the normal localization of the double images when the patient fixated with the usually deviated eye.

Not all patients are as adaptable as the one in the case just discussed. It is not surprising, therefore, that I have seen a large number of patients in whom occlusion of the better eye, carried out for months, had no influence whatever on the sensorial retinal relationship. Travers³⁴ had a similar experience in 5 cases, in which alternating occlusion of one eye over an average period of four and a half months was completely ineffective. One is forced to conclude that the same factors which modify the establishment of anomalous correspondence and influence its spontaneous postoperative development in the individual case are also active when occlusion is carried out.

In evaluating monocular occlusion as a therapeutic means for the correction of anomalous correspondence, one must keep in mind that

it is a negative rather than a positive procedure. Simultaneous binocular stimulation is prevented, but nothing is done to further actively the reestablishment of the normal sensorial relationships. This is attempted by the methods which are now to be discussed.

2 METHODS RESTORING THE NORMAL POSITION OF THE EYES (OPERATIONS)

If the biretinal stimulation is to restore the normal sensorial relationship between the two eyes, then the stimulus must fall on such areas in the two retinas that the awakening of normal correspondence is made possible. In other words, the position of the eyes must be such that an object point fixated with one eye is also imaged on the fovea of the other eye. In most instances this can be achieved only by operation.

Travers,³⁴ as well as other authors, have stated the opinion that operation is the most effective method so far devised for dealing with anomalous correspondence. Indeed, there is no doubt that development in the direction of normal correspondence frequently takes place after surgical intervention. The ideal goal—a stable normal retinal relationship evident in all tests—is, however, only rarely achieved.

What is the reason for this? Strabismus is a deep-seated disturbance of the neuromuscular apparatus of the eyes. Operations on the ocular muscles can affect directly only the mechanical conditions. These operations are crude procedures when compared with the fineness of the neuromuscular mechanism which comes into play in binocular fixation. An absolute parallelism of the visual lines for distance is hardly ever achieved by operation and is often not desired. Since normal fusional amplitudes are almost always absent in patients with strabismus, such persons are unable to correct the small deviations of the visual lines which remain after successful operation. Consequently, the condition for regaining normal correspondence, the simultaneous stimulation of the two foveas by the fixation point, is lacking.

Another factor which frequently works against the spontaneous reestablishment of normal correspondence is the age at which operation is performed. As far as the cosmetic result is concerned, there is no upper age limit for the operation, but there is no doubt that the prospect for a satisfactory functional result decreases rapidly with the age of the patient. A patient who is operated on in his teens is much less likely to regain spontaneously normal correspondence and binocular vision than one who is operated on at the preschool or the grammar school age. This has been emphasized by many writers, and with regard to retinal correspondence, particularly by Montalvan.⁴⁸ Travers³⁴ published con-

⁴⁸ Montalvan, P. El tratamiento ortóptico del estrabismo concomitante, *Rev. cubana de oto-neuro-oftal.* 6:97, 1937.

vincing figures on this subject and he also showed that not only the age of the patient at the onset of the strabismus but also the "percentage of life" during which the patient squinted has to be considered in this respect

Yet one still hears and reads frequently that one should not operate for strabismus before the patient is 12 or 14 years of age. This is erroneous. Every child with strabismus who comes to a physician's attention should have his eyes straightened before entering school or shortly thereafter. There are many reasons for advocating such a policy, the better prospect for a good functional result is one of the more important ones. The danger of a postoperative divergence can be avoided by proper choice and proper performance of operation and should not be a deterrent to early surgical intervention.

5. METHODS PRODUCING BIFOVEAL STIMULATION (PRISMS)

In order to produce the image of the fixation point simultaneously on the two foveas of a squinting patient by nonsurgical means, prisms may be employed. The use of prisms in the treatment of strabismus has been strongly advocated by some authors, particularly Sattler,⁴⁹ who has seen good results from prisms as strong as 22 Δ . Other authors have found them useful. Travers³¹ applied them with special regard to overcoming anomalous correspondence but found the results in his 4 cases most discouraging. The prisms were heavy, unsightly and expensive, the children did not like them and the parents were resentful. In 1 case Travers noted an increase in the angle of squint after the prisms were worn.

Travers' material is too small to justify one in drawing final conclusions from it. Prisms can be used, of course, only when the angle of squint is relatively small, but there is no objection to their use on theoretic grounds. If the patient is at all capable of regaining normal correspondence, the correct position of the images on the retina will undoubtedly be helpful. It must be admitted, however, that prisms *in praxi* are not always beneficial, and that they can even be detrimental. In a number of instances I have seen an occurrence similar to that described by Travers, in which the angle of squint increased as a result of the wearing of prisms. The amount of increase usually corresponded to the amount of prism power prescribed. Since the prisms were given only in cases in which the angle of squint was small (5 to 6 arc degrees) and corresponded to it in strength, this usually meant that the angle of squint had doubled as a result of the wearing of prisms.

49 Sattler, C. H. Erfahrungen über die Beseitigung der Amblyopie und die Wiederherstellung des binokularen Sehakts bei Schielenden, *Ztschr f Augenh* 63 19 1927

This interesting observation may be explained as follows. Patients with strabismus try to avoid simultaneous macular perception. If they are operated on with success, the mechanical conditions are altered in such a way that the faulty innervational factors which remain operative, at least for some time, are unable to produce a deviation. The patient successfully operated on will either yield and return at least partially to sensorial normalcy or will acquire sensorial anomalies adapted to the new motor conditions. If the bifoveal stimulation is achieved by the use of prisms instead of by operation, the faulty innervational factors will continue to operate on the faulty mechanical conditions present in every case of strabismus. As a result, the situation will be aggravated. In order to avoid bifoveal stimulation, the eyes turn until the same distribution of the retinal stimuli is reached which existed prior to the use of prisms. Consequently, the patient now has the same angle of squint with the prisms which he had before wearing them.

Such experiences should not discourage the use of prisms. They are valuable, particularly for the correction of vertical deviations. But it would be wrong to rely solely on prisms for the therapy of anomalous retinal correspondence. More active methods must be sought to encourage the establishment of normal correspondence.

4 METHODS EMPLOYING THE SIMULTANEOUS STIMULATION OF SELECTED RETINAL AREAS (ORTHOPTIC EXERCISES)

When the image of the fixation point is moved over the retina of the deviated eye, an anomalous localization of the double image may suddenly be replaced by normal localization. Bielschowsky^{31a} observed this in examining squinting patients with rotary prisms. When testing patients with the movable projection instrument,¹⁶ I have seen it happen time and again that normal correspondence would suddenly appear when a small light spot was moved to and fro on the screen in such a way that it was imaged on the region of the macula of the deviated eye.

The instability of the anomalous retinal correspondence and the fact that normal correspondence may be elicited by moving the image of an object over the macular area of the deviated eye are made use of in orthoptic training. It is known as "retinal massage."

According to Linksz,⁵⁰ the value of this treatment lies in the reconditioning of attention. As soon as the patient is able to catch two patterns in one act of attention, which is best achieved by flashing lights or by motion, they will appear in one and the same direction. This is undoubtedly an interesting explanation, the importance of attention in all functions of vision is paramount (Heering). It must not be overlooked, however, that for attention to be effective there must be a physiologic basis—in this instance the presence of common visual directions.

⁵⁰ Linksz, A. Objectives of Orthoptic Examination and Treatment, *Am J Ophth* 26 552, 1943.

Since I am dealing here only with the principles of treatment of anomalous correspondence, I shall not go into a discussion of the details of the orthoptic technic. But it must be pointed out that opinions about its value vary from complete denial to enthusiastic affirmation. Chavasse⁵¹ emphatically denied the possibility that a cure of anomalous correspondence could be achieved by means of orthoptic exercises, and Fowler⁵² found that orthoptic training was of no value either preoperatively or postoperatively in cases of abnormal retinal correspondence. On the other hand, one hears statements from some orthoptists that they effect a cure in virtually every case of anomalous correspondence. The truth, no doubt, lies between the two. It surely depends largely on the skill of the orthoptist what result will be achieved, but the over-all handling of the cases is just as important.

To awaken the normal sensorial relationship once, twice, or even three times a week for the short period during which the treatments

TABLE 1—*Influence of Orthoptic Treatment in Anomalous Correspondence in Operative Cases*
(After Berens, Elliot and Sobacke⁵³)

Orthoptic Treatment	Retinal Correspondence	Before Operation		After Operation	
		Number of Cases	Percentage	Number of Cases	Percentage
None	Normal	61	42	64	45
	Anomalous	83	58	80	55
Postoperative only	Normal	83	36	65	79
	Anomalous	30	53	18	21
Before and after operation	Normal	73	75	80	82
	Anomalous	25	25	17	18

are given, and to allow the patient to relapse into his faulty visual habits the rest of the time, will certainly not produce a cure of anomalous correspondence.⁵³ Provision must be made to prevent the patient permanently from the wrong use of his eyes.

The best method to achieve this is the operative correction of the angle of squint. All authors who agree that orthoptic training is beneficial in the therapy of anomalous correspondence are also agreed that it should be given in conjunction with operative procedure.⁵⁴

51 Chavasse (footnotes 27 and 46)

52 Fowler, M. J. Value of Orthoptic Fusion Training Exercises in Strabismus and Related Conditions, *Arch Ophth* 28 507 (Sept) 1942

53 A word of warning must be inserted against the indiscriminate use of home exercises with stereoscopes. I have seen a number of patients in whom anomalous visual habits had become thoroughly established owing to the uncontrolled use of a stereoscope.

54 T. Keith Lyle (Lyle, T. K., and others. Orthoptic Training, *Tr Ophth Soc U Kingdom* 59 491, 1939) expressed the belief that "the persistence of

In this connection, the figures published by Berens, Elliot and Sobacke⁵⁵ are of particular interest. These authors followed a large number of cases and found that operation alone hardly influences the condition of the sensorial retinal relationship. A return to normal retinal correspondence is found in a substantial number of patients if the operations are combined with orthoptic procedures. The figures given by these authors are reproduced in table 1.

In concluding this survey of the principles of treatment of anomalous correspondence, it can be stated that there is no one certain panacea for all cases. In fact, the treatment of this condition is one of the most difficult problems in ophthalmology. Even the most skilful application of all means at one's disposal leads to a permanent cure in only a relatively small number of cases. Again, all the factors which lead to the establishment of anomalous correspondence—the age of the patient, the individual adaptability and the completeness with which the normal correspondence is repressed—play a decisive role in the success of the treatment.

abnormal correspondence in spite of diligent orthoptic treatment over a period of two to three months indicates the necessity for operation in the hope that the retinal correspondence which occurs in some 40% of the cases may become normal."

55 Berens, C., Elliot, A. J., and Sobacke, L. Orthoptic Training and the Surgical Correction of Strabismus. A Comparative Study of Binocular Vision in 324 Surgical Cases With and Without Orthoptic Training, *Am J Ophth* 24 1418, 1941.

(To Be Concluded)

News and Notes

EDITED BY DR W L BENEDICT

UNIVERSITY NEWS

The University of Michigan Department of Postgraduate Medicine, Department of Ophthalmology—The twenty-first annual intensive postgraduate course in otolaryngology and ophthalmology will be given from April 24 to April 30, at the University of Michigan Medical School, Ann Arbor, Mich., by the resident staff and the following guest lecturers: Dr Albert D Ruedemann, Cleveland, Dr Dohrmann K Pischel, San Francisco, Dr Edmund B Spaeth, Philadelphia, Dr Jack S Guyton, Baltimore, Dr Elmer L Whitney, Detroit, and Dr Willis S Knighton, New York.

Applications or inquiries should be sent to the Department of Postgraduate Medicine, University Hospital, Room 2040, Ann Arbor, Mich. Owing to the difficulty of obtaining accommodations, it is wise to write at once for reservations to the Michigan Union, University of Michigan, Ann Arbor, or the Women's League, University of Michigan, Ann Arbor.

GENERAL NEWS

Optical Aids for Subnormal Vision—The Committee on Sensory Devices of the National Research Council has available a limited number of reprints of a condensation of the "Report on a Survey of Optical Aids for Subnormal Vision," by V S Ellerbrock, recently published in the *Journal of the Optical Society of America*. There are also available a limited number of copies of the original, unabridged, report. This report, which was prepared to guide the committee in formulating a program of research, deals with the theory and practical aspects of telescopic spectacles, loupes, reading glass magnifiers and projection systems, as well as with recommendations for possible improvements in these devices. Copies of either of these reports will be mailed to professionally interested persons, on request to the Dartmouth Eye Institute, 4 Webster Avenue, Hanover, N. H.

Oregon Academy of Ophthalmology and Otolaryngology—The eighth annual spring postgraduate course in ophthalmology and otolaryngology will be held in Portland, Ore., April 7 to 12, 1947. The Oregon Academy of Ophthalmology and Otolaryngology and the University of Oregon Medical School have arranged a program, and Dr John Dunnington, professor of ophthalmology at Columbia University College of Physicians and Surgeons, New York, and Dr George Shambaugh, professor of otolaryngology at Northwestern University Medical School, Chicago, will be the speakers. There will be lectures, clinical demonstrations and ward rounds. Preliminary programs will be available about March 1. Additional information may be procured from Dr Harold M. U'Ren, secretary, 1735 North Wheeler Avenue, Portland 12, Ore.

American Orthoptic Council—The next examination for technicians by the American Orthoptic Council will be held in September and October 1947. The written examinations will be held at various cities in the country on Friday, Sept 12, 1947. Only candidates passing the written examinations will be permitted to take the oral and practical tests, to be given in Chicago, Saturday, Oct 11, 1947.

Applications on the official form must be received before July 1, 1947.

Communications may be addressed to the American Orthoptic Council, 23 East Seventy-Ninth Street, New York 21.

Annual de Schweinitz Lecture—The 1947 de Schweinitz Lecture will be given on Thursday, Nov 20, 1947, in Philadelphia, by Dr Bernard Samuels of New York, whose subject will be "Necrosis of Intraocular Tissues."

SOCIETY NEWS

Election of Officers, American Academy of Ophthalmology and Otolaryngology—At the meeting of the American Academy of Ophthalmology and Otolaryngology in October 1946 the following officers were elected: president, Dr Alan C Woods, Baltimore, president elect, Dr C H McCaskey Indianapolis, executive secretary-treasurer, Dr W L Benedict, Rochester, Minn., secretary for otolaryngology, Dr O E Van Alyea, Chicago, secretary for ophthalmology, Dr Algernon B Reese, New York, secretary for instruction in otolaryngology, Dr Dean M Lierle, Iowa City, secretary for instruction in ophthalmology, Dr A D Ruedemann, Cleveland, secretary for home study courses, Dr Lawrence R Boies, Minneapolis, secretary for public relations, Dr Erling W Hansen, Minneapolis. Councillors elected were Dr C H McCaskey, Indianapolis, Dr James M Robb, Detroit, Dr C D Blassingame, Memphis, Tenn., and Dr W Ivan Lillie, Philadelphia.

Asociación para Evitar la Ceguera en México.—The Society for the Prevention of Blindness in Mexico will hold a third scientific week from Aug 11 to Aug 16, 1947, in México, D F. Papers are invited and should be in the hands of the Asociación para Evitar la Ceguera en México, Gomez Farias 19, Mexico, D F not later than July 10, 1947.

Correspondence

TEACHING OF BASIC SCIENCES IN OPHTHALMOLOGY

To the Editor—I have read with great interest the proof of Dr Cogan's article on "Aims and Aids in the Teaching of Basic Sciences in Ophthalmology"

Dr Cogan's insistence that "emphasis should be put on the teachers and the course organized around them" is admirable. His outline of the material to be covered in the basic sciences cannot but be helpful to any administrator organizing such courses, and little exception can be taken to the fundamental value of the program he has outlined. It is immediately obvious, however, that, bearing in mind the qualifications of instructors and the subject matter to be covered, such courses in basic sciences can be given only in medical centers where ophthalmology is a major department and the necessary teaching personnel is available. Even in such centers the content of these courses will almost undoubtedly vary according to the individual interests, talents and opinions of the teaching staff. This is well illustrated by the material suggested by Dr Cogan for the course in physiology—subjects in which Dr Cogan himself is preeminently interested and in which his own investigations have been most noteworthy.

Granted that the content of the courses given in various ophthalmologic research centers will vary considerably according to the qualifications and interests of the different faculties, there are still several questions to be considered. First, what is the value of such instruction to future interns in the average isolated ophthalmic hospitals? Second, can all the men who take these courses with the idea of becoming ophthalmologists ultimately be placed in proper internships in ophthalmology? Third, in the larger ophthalmologic centers, should this instruction be given preliminary to the internship, or should it be given as an integral part of the first year's training?

In answer to the first of these questions, unhesitatingly I should answer that such preliminary training would be of value to the future interns in the isolated ophthalmic hospitals and in the end would raise the standards of ophthalmology practiced in such hospitals. In many instances, such a course in the basic sciences would be the one opportunity of such interns to obtain insight into basic scientific ophthalmology. Even though the prospective ophthalmologist may be better grounded in the basic sciences than his future preceptors, and so be liable to a rude awakening when he begins his actual clinical training, nevertheless, the general level of ophthalmologic practice will be considerably raised by this program.

Concerning the second point, however, one cannot but harbor grave doubts. If entrance to these courses in the basic sciences is limited to men with the proper scientific background and to men who have already obtained internships in ophthalmology, full approval of the program is instantaneous. However, at the present time every ophthalmologic

institution is deluged with applications from would-be ophthalmologists. The reasons for this are obvious. First, in addition to the normal number of recent graduates who wish to become ophthalmologists and heretofore have comfortably filled the existing internships, there are a number of men who under normal conditions would have specialized in ophthalmology several years ago but have been delayed in starting their training by their military service. Second, there are a great number of poorly trained and educated men who have completed their military service, are dissatisfied with their former medical practice and now take the opportunity offered by the G. I. Bill of Rights to enter a speciality which they correctly believe to be lucrative and erroneously believe to be easy. The great majority of the latter group are poor material and even under normal conditions would have great difficulty in obtaining hospital appointments. Under present conditions their chances of so doing are minimal. It is unfortunate, but true, that as a rule the applications of the latter group wind up with the statement that they have been accepted for such and such a course in the basic sciences and will be available for appointment on a certain date. I have grave doubts whether any appreciable number of this group will ever succeed in obtaining the later necessary clinical training. When one considers the limited number of ophthalmologic internships available and the present overwhelming number of applicants, it would appear that many of the graduates of these courses are doomed to disappointment in their desire to become properly qualified ophthalmologists. Therefore, while I am in full approval of Dr. Cogan's proposition that men later entering isolated ophthalmic hospitals should have this course in the basic sciences as a preliminary, I feel strongly that admittance to such basic courses should be limited to men who have either obtained their ophthalmologic internships or who have fair prospects of ultimately being properly placed.

On the last question I have raised, namely, the wisdom of giving these courses as a preliminary to internship in the larger ophthalmologic research and teaching centers, I am in complete disagreement with Dr. Cogan's opinion that the courses should be taken by a student just prior to his residency in ophthalmology if possible, but in any case not during his residency. To my mind, the future ophthalmologist is vastly better able to appreciate the content of the basic science training if he is surrounded at the same time with evidences of its clinical application and if he realizes the necessity of a proper scientific foundation for his clinical work. For example, a student of ophthalmic pathology is more able to appreciate the significance of histologic changes when he has some inkling of the varying clinical course of the disease he is studying. Further, a student receives a stimulus from serving under an instructor in the wards of a hospital and then following the same man to his laboratory for basic training in the applied sciences. To see the knowledge he gains in his basic courses—physiology, bacteriology, chemistry, anomalies of ocular movements and stereopsis, anatomy and other sciences—directly applied to the actual care of the patient is to my mind much better training than straight didactic or laboratory instruction, divorced from clinical work.

In the larger ophthalmologic institutions such combined basic scientific and clinical instruction can be readily arranged. The internship

runs through an entire year, and practically all men continue for an additional year or longer. I believe the wisest plan for the training of ophthalmologists is to spread the basic work in anatomy, pathology, physiology, chemistry, physiologic optics, muscular anomalies, etc., throughout the first year of training and to continue into the second year more advanced work in pathology, bacteriology and other subjects which may be of especial interest to the individual student, thus allowing the young ophthalmologist an opportunity within certain definite limits, to develop along his own natural inclinations.

ALAN C WOODS M D Baltimore

Johns Hopkins Hospital

Having been interested in ophthalmologic education and the training of ophthalmologists for twenty-two years, it is my hope that the article by Dr. Cogan will act as a stimulus to better teaching. While I am in general agreement with the ideas expressed in this paper, I believe that a few points will bear discussion.

It is well known that many clinicians have an inadequate knowledge of the basic sciences as applied to ophthalmology having obtained their training by preceptorships or in an institution where only clinical practice is taught. Any courses in the basic sciences added to such teaching are of inestimable value.

For many years studies in the basic sciences have been an important part of the four year period of training in ophthalmology at the State University of Iowa College of Medicine. It has been felt that one not grounded in such subjects cannot be a good clinician. In addition the residents have been encouraged to enhance their knowledge of internal medicine, neurology and certain phases of pediatrics.

I am in agreement with Dr. Cogan in his belief that the teachers "either make or break the course." Most assuredly, the instructors should be clinicians, since only they can emphasize important medical and surgical points.

I cannot agree in the belief that the basic sciences should be studied necessarily prior to the residency in ophthalmology, and in no case during the period of residency. From long experience, it is felt that the preferable method is to train interns in the basic sciences and in clinical ophthalmology concurrently, preferably during the first two years of residency. Taught in this manner, the student is more stimulated to study, and by daily application, for example, of embryology, anatomy, bacteriology and pathology to clinical practice he is made to realize the importance of a thorough knowledge of the basic sciences. As a consequence, an inclination to study some of the "dry" subjects is created. It is the experience of my colleagues and myself that there is much more interest in the basic sciences when they are applied daily to clinical problems. For example, in the course in bacteriology, the student spends six months in the study of external diseases and bacteriology, during which time he makes smears, cultures and other laboratory tests on each patient seen in the clinic. Thus, the clinical and laboratory findings are correlated, and the entire picture is fixed in mind. Likewise, in the training in pathology a patient with malignant melanoma, for example, is examined in the clinic, and after removal of the eye gross and microscopic studies are made.

As to the amount of training in the basic sciences, it seems that twelve weeks is not sufficient. six months would be preferable

However, let there be training in the basic sciences, whether it is during, before or after the residency. More interest and willingness to sacrifice on the part of those who teach will result in a better profession

C S O'BRIEN, M D, Iowa City

I heartily approve of the basic course described by Dr Cogan. It is difficult to see how any one could disapprove of it, since "the proof of the pudding is in the eating" and the course has already been given so as to satisfy its students and teachers. Facts which Dr Cogan did not mention, but which I understand to be true, are that the course has been limited to thirty members, that many more applications have been received than could be accepted and that the course has been financed by tuition fees. For several reasons, the course should be of benefit to ophthalmologists and to ophthalmology. It will attract desirable men and exclude or discourage those obviously unsuited to become ophthalmologists. It will stimulate qualified men to undertake ophthalmologic research, and it will produce a reserve of future teachers. It will induce ophthalmologists who have taken it to read the literature in their field and will enable them to do so with pleasure and profit.

It is probable that at the outset the teachers will learn more from the course than will the students and that later the teachers will lose their enthusiasm. By the time they do so, however, new teachers may be available from the ranks of their former students.

In conclusion, I cannot refrain from noting that a paper which I wrote twenty-eight years ago (*Suggestions Regarding the Teaching of Ophthalmology*, ARCH OPHTH 49:1 [Jan] 1940), and which I read before the New York Academy of Medicine, Section of Ophthalmology, is just beginning to bear fruit.

F H VERHOEFF, M D, Boston

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I have read with interest the article by Dr David G Cogan entitled, "Aims and Aids in the Teaching of Basic Sciences in Ophthalmology." There is no question in my mind but that a study course in the basic sciences as applied to the eye will become a regular part of every ophthalmologic residency in the country. The experience gained in organizing the course at Columbia University and in participating in the course at Harvard and in the two courses sponsored by the Ophthalmological Study Council has given me a number of impressions which I should like to discuss in connection with Dr Cogan's paper.

I agree with Dr Cogan that only the exceptional person acquires adequate training in the basic sciences as applied to ophthalmology without an organized course. Without such a course the average resident enters ophthalmology with only a superficial knowledge of the applications of the basic sciences to the eye.

As Dr Cogan says, the success of the course depends in large measure on the faculty, and it is in connection with the faculty that most of the difficulties have arisen. In the course at Columbia it was originally planned that the basic science departments themselves should

furnish the principal instructors, these to be supplemented by instructors from the department of ophthalmology itself who had had special training in the basic sciences but who were primarily clinical ophthalmologists. It was soon found that unless the instructors from the basic science departments had developed special interests in the eye their management of the course proved generally unacceptable to the residents. These nonophthalmologic instructors tended to offer simply a review course in the basic sciences, without making any attempt to apply their knowledge to specific problems in ophthalmology. Generally speaking, it is not possible in any one school to assemble instructors who have special ophthalmologic interests in all the fields of the basic sciences. Some sort of compromise must therefore be made. Perhaps one method would be to stimulate interest in ophthalmic problems among the members of the basic science departments by offering adequate remuneration to the instructors for their time and effort. An alternative possibility would be to bring in instructors from other schools. Bringing in outside help has the advantage that superior instructors can be chosen who will be able to maintain the interest of the residents, but there is the great handicap that such instructors must in general rely wholly on didactic instruction, without the advantage of supplementary laboratory work. I agree thoroughly with Dr. Cogan that the basic course must have laboratory instruction in addition to the didactic work if it is to be truly successful.

There must be a happy balance between didactic instruction and laboratory instruction. A course heavily weighted on either side will be unsatisfactory. In this connection, it is of interest to refer to the two courses sponsored by the Ophthalmological Study Council, in which lack of adequate laboratory facilities was balanced in large part by the superiority of the teaching staff. This course, unlike the university-sponsored courses, had the benefit of outstanding instructors in each subject, imported from all parts of the country, whose enthusiasm and prestige were able to compensate in large part for the absence of laboratory facilities. It should be mentioned, however, that a certain amount of laboratory work was made available in the second of the Council's two courses. At the other extreme is the course too heavily weighted on the laboratory side, in which much valuable time is lost in conducting useless experiments and with which the students become exhausted and bored. Much greater skill is required on the part of the instructor in handling the laboratory demonstrations than in ordinary didactic instruction. It is often better to have the experiment performed by the instructor in front of the class than by the individual members of the class. Students in ophthalmology should not be returned to the freshman level of medical study.

The value of weekly examinations was well shown in the courses of the Ophthalmological Study Council. Knowledge that the examination was to be given on the material currently presented served as a healthy stimulant to the student, and returned papers with corrections served to point up deficiencies. The grades in these courses should be saved for presentation to the American Board of Ophthalmology, to be used as an aid in determining the fitness of applicants for examination.

I agree with Dr Cogan that the proper time for the basic science course is just prior to the beginning of the residency. Experience at Columbia University showed that it was highly undesirable to have the course run simultaneously with the clinical work. Inevitably, calls from the wards and clinic obtained priority over calls from the course. This does not mean in any sense that training in the basic sciences should be discontinued during the residency. Ocular pathology, for example, is a subject which must have continuous application, as in weekly pathologic seminars, to enable the resident student to correlate his clinical and pathologic observations. Ophthalmic bacteriology is another subject which must have continuity and is best taught by requiring the resident to participate in a clinic for external diseases and to make his own cultures and microscopic slides.

Finally, every effort should be made in the university eye clinic to turn the interests of the younger men toward the basic sciences. In the past, pathology has received the greatest attention, but there is no reason that each university staff should not have an ophthalmologist qualified to teach and do experimental work in each of the basic sciences. There should be no hesitancy in calling on the basic science departments themselves for aid in the course, but I wish to stress again my belief that only exceptionally can the nonophthalmologic instructor in the basic sciences furnish the liaison between his science and ophthalmology that is absolutely essential.

PHILLIPS THYGESON, M D, Los Altos, Calif

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I was very much interested in Dr Cogan's article on the teaching of basic sciences in ophthalmology.

The outline is that of a truly basic course and is more comprehensive in the fundamentals than is usual in such courses. Any university that offers similar studies will be delighted with the outline presented. The division of hours is somewhat like that given at Washington University School of Medicine.

Of particular value is the apparent participation of the student in the laboratory work. Not only would twelve weeks of purely didactic teaching be unbearable, but the material would be poorly absorbed. It is only by delving into subjects with hands and eyes, as well as ears, that true understanding is gained and facts and theories are digested sufficiently for their retention.

My criticism of a purely basic course that does not include pathology and refraction is that it does not prepare a man adequately for the residencies that are now available in nonteaching institutions, since in most of these hospitals there is one to teach such subjects satisfactorily. The result is usually that the resident in ophthalmology learns his refraction by "hit or miss" methods, reading textbooks and occasionally picking up a few words of advice from a busy visiting staff ophthalmologist. He generally gets no instruction at all in pathology. Other subjects might be mentioned, such as muscle studies, orthoptics and practical perimetry, which need to be taught personally. It is agreed that these are not basic subjects, but they cannot be picked up and well understood without more definite instruction than a resident is likely to get in most hospitals.

For these reasons, it has seemed to me that the basic sciences in ophthalmology should be taught along with the clinical instruction. Therefore, at Washington University the so-called basic course, of eight months, has been a combination of basic and clinical training, approximately two hours a day being devoted to the basic work and six hours to clinical studies. This, to me, is the ideal arrangement, and I strongly favor it when possible.

The giving of a splendid basic course, such as Dr. Cogan has outlined, is indeed of great value, and the intelligent student will be able to build satisfactorily on it. But he will be indeed fortunate if he can later find a residency where he will receive systematic instruction in the clinical subjects.

LAWRENCE T. POST, M.D., St. Louis

Washington University School of Medicine

The aims of the basic science course in ophthalmology which Dr. Cogan has outlined are ideal. Any good student fortunate enough to take such a course given by Dr. Cogan and his associates should not only be thoroughly grounded in fundamental subjects but should also have acquired some knowledge of experimental methods. Association with such a group could not help but stimulate his curiosity, and it is more than likely that from it many top-ranking clinicians with an investigative turn of mind would eventually be produced. One cannot emphasize too strongly, however, as Dr. Cogan has only modestly hinted, that the success of such a course depends entirely on the personnel of the department giving it. There are not many institutions in this country in which a similar group of men form a staff capable of presenting such a course and having sufficient time to conduct it personally. To be realistic, there are probably not more than six residencies in this country in an institution where such a course could be given.

I made the statement that any good student accepted for this course would be fortunate. By the term "good student" I mean one who is suitable. It must be recognized that not all physicians who wish to become ophthalmologists have the same objectives, interests or capabilities. The course which Dr. Cogan has outlined is designed only for those students of superior mental caliber who have an interest in the academic aspects of ophthalmology, as well as its practice, and who hope eventually to become associated with a teaching institution where research is done. For any other type of student the laboratory work in physiology proposed in this paper would be ill suited.

Fifteen years ago I organized such a course for the students in the graduate school of ophthalmology at the University of Pennsylvania. It was limited to the physiology of the eye. My thought was to have the students repeat in the laboratory some of the sound experimental work in the older literature which had yielded proved ideas incorporated in present day thinking, so that the student could see for himself how present conceptions had been arrived at. Considerable time and thought were expended on setting up a series of experiments which could be performed by a small class without much previous experience in laboratory work. The results were disheartening. Out of a class of approximately 15 men, there were 2 or 3 who may have benefited. The others carried out the laboratory instructions fairly satisfactorily but showed little understanding of what the experiment was intended to prove and

no interest or initiative in carrying the reasoning of the experiment further. Most of these men were good students, but their chief interest was in practical ophthalmology. They had had no laboratory experience, and their powers of reasoning from experimental data had never been developed. The failure was not theirs, but mine, in that I had not selected the type of man from the class who would have benefited.

I am skeptical, therefore, whether the course as outlined by Dr Cogan will have very widespread usefulness. To be successful, it must be limited to just the type of man who benefits from this kind of instruction.

In the residency in ophthalmology at the University of Pennsylvania Hospital, the basic sciences are taught in the Graduate School of Medicine during the first eight months of the residency. While the students do laboratory work in anatomy, embryology, histology, pathology and physiologic optics, no laboratory periods are given in either physiology or chemistry. By the time the resident has been with us for two years, my colleagues and I have had an opportunity to determine whether or not he is the type to do experimental work. The men showing the mental qualifications and interest are then selected in the third year, when they carry on research with the various members of the staff and eventually are given problems of their own.

To summarize, I believe Dr Cogan's course is ideal if given by a staff similar to his to students whose mental capacities and interests are suitable. It will not have widespread application, because there are not many institutions where a similar group of trained teachers are to be found who have the time to give twelve weeks to the presentation of such a course. Further, the number of men who will be found suitable for this type of teaching is small.

FRANCIS HEED ADLER, M.D., Philadelphia

313 South Seventeenth Street

Dr David Cogan's discussion of the "Aims and Aids in the Teaching of Basic Sciences in Ophthalmology" offers much valuable help to those who are planning the organization of such courses. I agree with him that an increasing number of institutions will require such training as a prerequisite to clinical residency. Of those institutions which do not insist that such training be completed before the appointment to the residency is made, an increasing number will require some such instruction as part of the resident training program. At every stage in training and practice those who have had such a review demonstrate its advantages.

With Dr Cogan's aims I am in entire agreement. Two of his conclusions (relating to the teaching staff and the period of the course) will probably be challenged, but the difficulties which my associates and I have encountered in conducting a review of the basic sciences at Columbia have led us to share his convictions.

The Faculty—It is evident that facilities for teaching a comprehensive review course in the basic sciences are at present to be found only in the large teaching centers. Since the other medical specialties are also interested in promoting training in the basic sciences for future residents in their specialties, several medical schools have organized

basic science faculties, usually operating under the dean or the associate dean in charge of graduate instruction. There is such a basic science faculty at Columbia University, and it was our hope to use this faculty, in common with the other specialties, for instruction in the basic sciences in ophthalmology. This hope has not been fulfilled. Members of the basic science faculty who were not ophthalmologists or who had not acquired special interests in this field did not seem to realize the problems associated with ophthalmology or to fulfil the highly specialized needs of the course. There was too much extraneous material unrelated to ophthalmology, and too often the teaching was simply of first or second year medical school caliber.

Another plan proposed the utilization of three or four full-time members of the ophthalmologic faculty to do all the teaching. In periods between basic science courses these faculty members would devote full time to laboratory direction or studies. This plan has serious disadvantages. It is difficult to find an adequate teaching staff with the deep interest in and enthusiasm for all the subjects to be covered. The teaching tends to become too didactic and academic.

In our experience, the use of members of the clinical attending staff who are actively practicing ophthalmology, supplemented by the assistance of the full-time nonclinical staff, has proved most satisfactory. It distributes the teaching over a large number of men and assigns to each the subjects in which he has special training and interest. At the end of each course reports received from faculty members on the caliber and performance of the students are evaluated, together with similar reports from students on the instructors and material, with a view toward modifying the content or arrangement of the subsequent course.

The Time—I agree with Dr. Cogan that the course should be taken just prior to, but not during, the residency. If properly organized and conducted, the review course in the basic sciences is a full-time occupation for several months, and it is my feeling that it should not be undertaken when other demands on time and attention are likely to cause conflicts. By other demands I mean, for example, calls to the ward to take histories or make physical examinations, to perform laboratory tests or to act as assistant. The student should have maximum freedom from responsibility and maximum opportunity for diligent application. The pursuit and application of his basic science studies can and should be carried on into his period of residency, and many of the short items in the curriculum can well be placed in both the basic science and the resident training schedule.

Dr. Cogan's outline of the content of the Harvard course is practical and well balanced. At Columbia we assign a higher percentage of time to bacteriology and virus studies, a lower percentage to neurology and neurophysiology and a considerably higher percentage to miscellaneous studies (such as biostatistics, diagnostic tests, ophthalmologic histories and examinations and evaluation of clinical and scientific problems). Within moderate limits, the time assigned to each subject will vary with the facilities—faculty, clinic and laboratory—for teaching it. My feeling at present is that a good comprehensive review in the basic sciences can be given in a full-time four months' course,

of approximately eight hundred hours, about four hundred of which are given to lectures and laboratory work

There is a wide divergence of opinion between those who take the "let them dig it out for themselves" attitude and those who believe that every conference hour should be carefully prepared for, summarized and evaluated. While one is not dealing with preparatory school students or medical undergraduates, I firmly believe that the amount of material to be covered in four months requires careful faculty preparation and considerable discussion. The faculty member is in a much better position to evaluate the present status of knowledge than is the student, particularly with reference to sources of material. At Columbia we allot about one-half the time (four hundred hours) to study periods, not counting evenings, and divide the other four hundred hours between laboratory work, with demonstrations, and lectures, conferences, discussions, quizzes and seminars. Didactic work may be supplemented with examinations, quizzes or, preferably, seminars, in which students prepare, discuss and defend theses. Six review periods are conducted by an administrative officer (we use the director of research), who can direct or encourage individual investigations into fields for which the student has special talent or training.

The preparation of laboratory outlines, including notes, notebooks, photographs, bibliographies and reprints in each subject, has proved of great help in systematizing the material covered. So many laboratory data (chemical formulas, preparation of stains, details of technic, optical equations and formulas and tabular data) are so easily twice learned and thrice forgotten that this material should be stored in a place where it is immediately available when needed. In this way, the student's mind and attention can be freed for more important aims: the development of a breadth of view, clear thinking and careful observation, with critical analysis or evaluation of what he sees, reads and hears.

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Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Congenital Anomalies

PERSISTENCE AND HYPERPLASIA OF THE PRIMARY VITREOUS A B
REESE and F PAYNE, Am J Ophth 29:1 (Jan) 1946

Reese and Payne attribute the increased frequency of retrolental fibroplasia to a lower mortality of premature babies. They describe four clinical types of this condition, and report 50 cases. They discuss these from the standpoint of diagnosis, the embryologic, pathologic and etiologic aspects, and treatment.

W S REESE

CONGENITAL ANOMALIES FOLLOWING MATERNAL RUBELLA IN EARLY WEEKS OF PREGNANCY, WITH SPECIAL EMPHASIS ON CONGENITAL CATARACT C H ALBAUGH, J A M A 129:719 (Nov 10) 1945

Albaugh reviews the literature and reports 9 cases of congenital abnormalities in the infant following an exanthem in the mother in the early weeks of pregnancy. The following summary is supplied. Available data suggest that 100 per cent of the mothers who contract rubella in the first two months, and approximately 50 per cent of those who contract it during the third month of pregnancy, will give birth to infants with congenital anomalies.

The commonest lesions in the infants are cataract, cardiac septal defects and patent ductus arteriosus, deaf-mutism and microcephaly.

Nearly all the infants are poorly developed and are feeding problems.

W ZENTMAYER

General

MOSCOW EYE HOSPITAL A USPENSKY, Brit J Ophth 30:372 (June) 1946

Uspensky gives a brief description of the Moscow Eye Hospital, one of the oldest ophthalmologic institutions in the country. It was founded one hundred and twenty years ago. The outpatient department is visited daily by 500 patients. The number of beds is 250. The hospital has adjunct clinics for thorough special examinations of the patients. It holds periodic and regular scientific conferences for exchanges of experience and maintains close contact with related institutions.

W ZENTMAYER

General Diseases

OXYCEPHALY ASSOCIATED WITH KLIPPEL-FEIL SYNDROME AND OTHER SKELETAL DEFECTS A L PETER, Am J Ophth 29:685 (June) 1946

Peter reports 4 cases of mild oxycephaly in which skeletal defects were present. The chief complaint in all cases was inability to wear

the ordinary type of helmet. He presents these cases to show that this condition exists in mild form and shows few, if any, symptoms.

W S REESE

OCULOGLANDULAR TULAREMIA A A SINISCAL, *Am J Ophth* 29: 698 (June) 1946

Siniscal reports 3 cases of proved oculoglandular tularemia, in all of which a domestic animal which had been previously ill was deemed the agent of transmission, although it was impossible to determine positively that the animal's illness had been tularemia.

W S REESE

General Pathology

A CONTRIBUTION TO THE PATHOLOGY OF BOWMAN'S MEMBRANE
A LOEWENSTEIN, *Brit J Ophth* 30: 317 (June) 1946

Loewenstein studied the histologic changes in Bowman's membrane in a case of band-shaped corneal degeneration and in glaucomatous eyes, as well as the concretions in Bowman's membrane in a case of late changes following mustard gas (dichloroethyl sulfide) injury to the eye and in a case of hypertensive retinopathy. He concludes that precipitation of calcium phosphate in Bowman's membrane may be due to a slowing down of corneal metabolism. Carbon dioxide escapes, alkalosis sets in, and calcium phosphate is condensed in the tissue with the slowest metabolism, which is Bowman's membrane. The influence of light in this process of precipitation is likely. A calcified Bowman's membrane is an obstacle to the exchange of normal fluid from the epithelium to the anterior chamber. Its sequel is the establishment of an amorphous eosinophilic substance in front of Bowman's membrane, which was observed in a case of band-shaped corneal degeneration and in a case of late, progressive macular corneal opacities after mustard gas (dichloroethyl sulfide) poisoning. Increased intra-ocular pressure may be a further obstacle to the entrance of fluid into the inner eye. The frequency of hemispherical bodies in Bowman's membrane in cases of primary and secondary glaucoma may be due to the precipitation at this border zone. A case of arterial hypertension is described in which another form of purple-staining concretions was present in Bowman's membrane and in the superficial scleral layers. The precipitation may be a general metabolic deterioration of the ocular walls.

W ZENTMAYER

Injuries

AN ANALYSIS AND FOLLOW-UP OF 301 CASES OF BATTLE CASUALTY INJURY TO THE EYES G I SCOTT and I C MICHAELSON, *Brit J Ophth* 30: 42 (Jan) 1946

Three hundred and one cases of battle injury to the eyes were analyzed and the men followed until they either were repatriated or had returned to duty.

Fifty-eight patients (19 per cent) had bilateral injury, 23 (76 per cent of the total number and 40 per cent of the men with bilateral injury) becoming certifiably blind.

In approximately 80 per cent of cases of injuries caused by grenades, land mines or booby traps the explosion occurred within 3 yards (27 meters). In approximately one third of cases of foreign bodies situated in the vitreous extraction was done with the electromagnet by the posterior route.

In 40 per cent of all cases of severe injury to the eye useful vision was retained, acuity being 6/12 or better in 20 per cent. In an additional 16 per cent, however, the defect was due to uncomplicated cataract, the eye being therefore potentially useful.

The final visual acuities in cases of perforation, contusion and concussion are compared, concussion being less destructive than contusion and perforation being considerably more serious than either in its effect on function.

A distinguishing feature is indicated between the clinical findings in cases of air-conducted and in cases of tissue-conducted concussion injuries to the globe. The pathogenesis of this distinction is suggested.

The principal causes of serious visual defect (6/60 or less) in cases of perforation, contusion and concussion are summarized. Infection appeared to be a negligible factor.

No case of sympathetic ophthalmia is recorded.

A follow-up study of 249 cases showed that over 60 per cent of the men returned to full duty.

W ZENTMAYER

AMNIOTIC MEMBRANE GRAFTS IN CAUSTIC BURNS OF THE EYE (BURNS OF THE SECOND DEGREE) A SORSBY and H M SYMONS, Brit J Ophth 30:337 (June) 1946

The authors feel that in the absence of control clinical or experimental evidence the results recorded here must be taken as an expression of clinical opinion, rather than proof. Most caustic burns are of the second degree. These burns show a localized and relatively superficial conjunctival lesion and a variable superficial corneal lesion. For these burns, which are both common and productive of much disability, grafting with amniotic membrane appears to offer a simple means of considerably reducing the normally protracted course of recovery and preventing both corneal and conjunctival complications. Thirty patients were treated with human amniotic membrane. Recovery was rapid, and there were few complications and sequelae. Grafting immediately or after one or two days is advocated for second degree burns of the eye.

W ZENTMAYER

Instruments

AN EXOPHTHALMOMETER FOR DIRECT MEASUREMENT A GORMAZ, Brit J Ophth 30:350 (June) 1946

The instrument consists of a metal millimeter rule carrying one fixed and one movable vertical stem resting on the outer orbital canthus. A central movable vertical stem, calibrated in millimeters and terminating in a shallow cup, can be moved into position over the eye to give the measurement of the projection of the corneal apex beyond the level of a plane formed by the two orbital canthi. In no normal case has the summit of the cornea as determined by these readings been

less than 12 mm above the fixed bony landmark of the outer orbital canthus. Generally the reading is 14 to 16 millimeters. The article is illustrated.

W. ZENTMAYER

Lens

SIMULTANEOUS DETACHMENT OF THE CHOROID AND RETINA AFTER CATARACT OPERATION H. ARRUGA, Barcelona, Spain, The Author, 1946

1 The author corroborates the frequency with which the retinal detachment occurs at the same time as the choroidal one, as pointed out by Bonnet and Grand-Clément.

2 The posterior or lateral location of the retinal detachment is always next that of the choroid, a fact suggesting that the exudate, instead of occupying the subchoroidal space, is situated under the retina and raises it.

3 The retinal detachment disappears at the same time that the choroidal one does, therefore, the two have the same benign and transitory character.

4 The pathogenesis of the two kinds of detachment is probably the same, with the difference that the extravasated fluid collects in the subchoroidal space in the one and on the inner surface of the choroid in the other.

5 In 1 case in which a true detachment of the retina occurred, two and one-half months after the operation, the position of the tear was an indication of its lack of relation to the postoperative detachments of the choroid and retina.

HUMBERTO ESCAPINI

CORNEAL SECTION AND SUTURES IN THE CATARACT OPERATION H. ARRUGA, Barcelona, Spain, The Author, 1946

The section in the limbus with conjunctival sutures heals quickly, but the union is not firmly closed against intraocular pressure and blepharospasm. The sutures are easily inserted and removed and if tied tightly fall out of themselves after six days. A stronger closing but a slower cicatrization of the wound is found when corneal or corneoscleral sutures are used. Very fine needles are necessary. The threads are sometimes difficult to extract. If the section is in the periphery and scleral, there is a tendency to hemorrhage from the vessels as they cross the anterior scleral region. When the incision is made in the limbus and the sutures include the cornea, sclera and a part of the conjunctiva, the union is solid, the healing is rapid and removal of the sutures is relatively easy.

ARNOLD KNAPP

Methods of Examination

THE ULTRA-VIOLET OPHTHALMOSCOPE J. DEMENT, Brit J Ophth 30:370 (June) 1946

The instrument consists of a round mirror, either concave or plane. Mounted in the central perforation of the mirror is a small circular window of an ultraviolet opaque medium, such as Noviol glass or Wratten 2-A filter. Behind this, on a rotor, may be mounted one or

more filters of transmission suitable for special observations, such as color analysis by filter radiometry. The ophthalmoscope is used exactly like its conventional counterpart. A source of filtered ultraviolet light (of "long wavelength," i.e., 3,650 angstrom units) is placed behind the plane of the subject's face, and the beam is directed toward the reflecting mirror, which is held in the line of vision of the subject and directed into the eye. There appears to be a number of interesting possibilities for use of the ultraviolet ophthalmoscope in medical and biologic science, not only for study of the internal ocular structures but for examination of such exposed regions as the brightly fluorescent sclera.

W ZENTMAYER

Neurology

BITEMPORAL HEMIANOPSIA W O LODGE, *Brit J Ophth* 30 276 (May) 1946

Lodge reports 3 cases of bitemporal hemianopsia. The first case was that of a girl aged 15 years with bilateral papilledema and Frohlich's syndrome. Only the inferior nasal quadrants of the fields of vision were intact. A diagnosis of adamantinoma was confirmed histologically. The tumor was removed by a transfrontal operation. The patient died of a recurrence of the growth. The second case was that of a man aged 35. The left field of vision showed a complete temporal defect. The right field showed a central scotoma without peripheral hemianopsia, the optic disks were pale. The tumor proved to be a meningioma of the olivary eminence of the sphenoid bone. It was successfully removed, but the patient died one year later of a recurrence. The third case was one of chromophobic adenoma in a woman aged 28. The fields showed bitemporal hemianopsia. A paranasal operation was performed and a radon seed inserted. Five years later papilledema was present, and bitemporal hemianopsia recurred. The tumor was removed. One year later there was little vision in the right eye, but on the left side vision was normal. The author's approach to intrasellar tumors is a modification of the Chiari operation. The article is illustrated.

W ZENTMAYER

Ocular Muscles

AMBLYOPIA EX ANOPSIA IN THE ARMED FORCES G E MORGAN, *Am J Ophth* 29:713 (June) 1946

Morgan analyzed 77 cases of amblyopia in the armed forces and found that the loss of vision was associated with strabismus in 56 per cent and with marked anisometropia in 30 per cent, in the remaining 14 per cent no associated etiologic factor was noted. Almost one-half the patients were seen by an ophthalmologist before the age of 7 years.

W S REESE

THE TREATMENT OF CONVERGENCE DEFICIENCY, 1933-1944 S MAYOU, *Brit J Ophth* 30:354 (June) 1946

The purpose of this somewhat lengthy article is to outline the progress made in the treatment of convergence deficiency at the Central London Ophthalmic Hospital during the past eleven years and to set

out, in somewhat greater detail, the methods developed by the author which are now employed to treat it. The subject is discussed under the headings of development of treatment, comparative methods of treatment, symptoms and causes, the psychologic approach to treatment, detailed treatment and conclusions. Under the last heading, the author states that the number of patients of all ages with convergence deficiency is large and that the symptoms, which may include migraine, are extremely unpleasant, the psychologic element is often present, and particular attention must be paid to the patient's mental approach both before and during treatment, since the successful remedy lies largely in his own hands. Care should be taken when testing and treating a patient with an esophoria, since many of these persons have a convergence deficiency as well. Even patients who are orthophoric and can actually converge may benefit from treatment, while many patients with small refractive errors are able to dispense with their correction after they have been treated. Above all, treatment can be quick and effective—on an average, two tests and five half-hour lessons—but must be taken under trained supervision, it should aim at building up voluntary convergence and teaching the patient to relax once convergence is established, since voluntary convergence alone can prevent a recurrence of the symptoms in after years. If a patient is discharged as cured after undergoing the treatment described in this article, it may be said with some certainty that, with the exception of the patient with symptoms of migraine, who may need a subsequent refresher course, the risk of his having to return for further treatment is infinitesimal.

W. ZENTMAYER

Parasites

OCULAR MYIASIS. R. E. GIQUEAUX and R. GARCIA OCHOA, *An argent de oftal* 5:79 (July-Sept) 1944

A discussion of myiasis in general is given. The subject of ocular myiasis is then treated, and the case of a baby 3 months old is reported. The baby was otherwise normal except for some tumefaction around the right ear. The right eye showed congestion, more intense at the caruncle and the semilunar fold. The mother had noticed that a worm came out at the inner angle and sank again into the tissues. The author could not see the worm, but by bringing a piece of cotton wet in chloroform to the inner canthus he could verify the presence of typical larvae embedded in the tissues. Worms were also found in the right ear by an otologist. All the larvae were removed by applying a cotton pledget wet in chloroform to the eye, and the child recovered uneventfully except that the conjunctivitis produced by the application of chloroform lasted for some time.

H. F. CARRASQUILLO

Pharmacology

DETERGENTS OR WETTING AGENTS. R. J. ROTH, *Am J Ophth* 29:717 (June) 1946

Roth reviews the physical and chemical characteristics of wetting agents and cites two properties that could be utilized by ophthalmologists, namely, (1) increased solubility of the drug in a solution of the proper

detergent, permitting a higher concentration of the drug in solution to come in contact with the eye, and (2) increased corneal permeability

W S REESE

Refraction and Accommodation

REPORT FROM THE WILMER INSTITUTE ON THE RESULTS OBTAINED
IN THE TREATMENT OF MYOPIA BY VISUAL TRAINING A C
WOODS, *Am J Ophth* 29:28 (Jan) 1946

Woods concludes from this interesting study of 103 persons with myopia that, with the possible exceptions of educating some patients to interpret blurred retinal images more carefully and of convincing some others that they could see better even though there was no actual improvement, the visual training given these patients was of no value for the treatment of myopia

W S REESE

Retina and Optic Nerve

MALARIA THERAPY IN SYPHILITIC PRIMARY OPTIC ATROPHY W L
BRUETSCH, *J A M A* 130:14 (Jan 5) 1946

From the microscopic study of the visual pathways in 70 cases representing all types of syphilis of the central nervous system, it became apparent that primary syphilitic atrophy of the optic nerve is due to a chronic inflammatory process followed by degeneration of the nerve fibers. One of the most important effects of malarial therapy consists in arresting the inflammatory phase of the neurosyphilitic process.

Malarial therapy, besides changing the tissue immunity, inhibits the inflammatory elements of syphilitic optic nerve atrophy, and the secondary degeneration of the nerve fibers ceases. In favorable cases one course of malaria treatments will suffice. If visual failure continues to progress, one should contemplate another course of malarial therapy. Quartan malaria (*Plasmodium malariae*) will have to be used, since in the interim immunity has developed to the tertian strain, with which the patient was previously inoculated.

To follow up malarial therapy with injections of penicillin or to give the drug concomitantly may be worth while. To rely on penicillin alone is hazardous. Routine antisyphilitic treatment is entirely inefficacious for syphilitic optic nerve atrophy, and the patient will become blind almost as rapidly as though he had received no treatment at all.

W ZENTMAYER

RETINAL HEMORRHAGES IN APLASTIC ANEMIA R J BUXTON, *Brit J Ophth* 29:632 (Dec) 1945

The patient, a Basuto aged 28, was receiving treatment for syphilis. The blood picture was that of aplastic anemia. There was no regeneration of blood cells. The optic disks showed blurring of the upper nasal edges only. The retinal vessels were normal in size and contour, with slight haziness of outline near the disk, the retina was pallid, and there was some edema about the disk. Three types of retinal hemorrhages were noted: (1) moderate-sized, flame-shaped plaques, up to 2 disk diameters in length, some with a yellowish center, which at times

glistered slightly, (2) narrow streaks about 1 disk diameter long, close to the blood vessels and (3) two or three petechial hemorrhages and one small area of exudate in the macular region

The article is illustrated

W ZENTMAYER

OCULAR SIGNS IN THE PRISONER OF WAR RETURNED FROM THE FAR EAST G C DANSEY-BROWNING and W M RICH, Brit M J 1:20 (Jan 5) 1946

Of the 30 men who were released at the recapture of Rangoon, who had been prisoners of war from two to three years, 27 had beriberi. These men were examined for their ocular symptoms. Ten had bilateral central scotoma. The periphery of the field was not contracted, vision could not be brought up beyond 6/60. Examination of the fundus revealed pallor of the disks, which included primary atrophy of the optic nerve in 4 men, pallor of the papillomacular bundle in 4 and pallor of the temporal half of the disk in the remaining 8. Not 1 of these 30 men examined showed ocular symptoms of ariboflavinosis, while during the same period 2 men from the German prison camps who had not had beriberi had a definite increase in limbal vascularization.

The scotoma extended from the point of fixation to the enlarged blindspot and presented a tail. The authors cite the modern theory of the causation of tobacco-alcohol amblyopia, namely, that the condition is due to a deficiency of thiamine, at the same time, they agree to the fact that the exact nature of the deficiency of nutritional neuritis remains obscure. They think that there is a relationship between the scotoma in these cases of beriberi and the scotoma of the toxic amblyopias. As the optic nerve is a part of the central nervous system, the damage done to the nerve proper by the axial optic neuritis of beriberi is final, and any improvement of vision can be but slight.

ARNOLD KNAPP

THROMBOSIS OF THE CENTRAL VEIN DUE TO TRAUMA. REPORT OF A CASE R BRUCKNER, Ophthalmologica 109:203, 1945

A man aged 40 sustained two contusions of the right eye within a week. Two months later partial obstruction of the central vein occurred in this eye. The patient had been in excellent health, and no cause could be found to account for the lesion. The author assumes that the venous obstruction was due to trauma.

F H ADLER

PRINCIPLES IN SURGICAL TREATMENT OF RETINAL DETACHMENTS M ROSENBLUM, Vestnik oftal 25:10, 1945

About 1,000 operations for retinal detachment have been performed since 1933 at the von Helmholtz Institute. The Gonin and Lindner methods, which were first used, gradually gave way to diathermy. Successful results were obtained in 54.3 per cent. The patients were followed for several years. The advantages and disadvantages of various methods and operations for detachment of retina are discussed.

O SITCHEVSKA

Trachoma

INCIPIENT PANNUS AS A SIGN OF THE PRIMARY CORNEAL INFECTION OF TRACHOMA AND AS AN IMPORTANT CRITERION FOR THE EARLY DIAGNOSIS OF THE DISEASE P K KUO, *Am J Ophth* 29:645 (June) 1946

Kuo discusses the difficulties in diagnosis of trachoma and states that careful examination with a loupe and focal illumination usually reveals neovascular sproutings from the pericorneal vascular loops of the upper overhanging limbus into the transparent part of the cornea

W S REESE

Tumors

TRANSCRANIAL REMOVAL OF INTRAORBITAL TUMORS J G LOVE and W L BENEDICT, *J A M A* 129:777 (Nov 17) 1945

In a consecutive series of 35 cases of intraorbital tumor, the transcranial approach through the roof of the orbit afforded excellent visualization of the pathologic growth and the important structures within the orbit and permitted removal of tumors which it would not otherwise have been possible to remove. There was only 1 death in the series, and the results generally were good.

The Kronlein operation is useful in removal of tumors of the optic nerve without enucleation of the eyeball or in removal of encapsulated tumors situated near the apex of the orbit. For removal of tumors in this region a transcranial approach is usually to be preferred. The choice of approach must, however, at times be determined by a factor other than that of accessibility. If further decompression of the orbit is desired, it is hardly possible to get the required resection of bone with Kronlein's method, whereas by the transcranial approach not only can the entire roof of the orbit and the optic canal be removed but the lateral wall can also be resected as far as necessary.

For removal of tumors that are definitely confined to the orbit, even in the posterior third, the frontal, or the Kronlein, operation may be adequate, as has been proved many times. However, one seldom can be certain that a tumor known to be in the apical portion of the orbit does not extend beyond the orbital walls, or where its origin may be.

This paper further emphasizes the comment made by Adson and Benedict in their report of a case in which a hemangioendothelioma of the orbit was removed through a transcranial approach (*ARCH OPHTH* 12:484 [Oct] 1934). "The ease with which the hemangioendothelioma was removed suggests many possibilities for the transcranial approach to vascular and neoplastic lesions situated in the retrobulbar space of the orbit."

The article is illustrated

W ZENTMAYER

TUMORS OF THE REGION OF THE LACRIMAL SAC P DESVIGNES and G OFFRET, *Arch d'opht* 5:25, 1945

Malignant tumors in the region of the lacrimal sac are rare. The authors describe 2 cases of epithelioma, in 1 of which operation had previously been performed and a small piece of the sac left. The second was a more recent case, in which histologic study revealed an epithelioma

The diagnosis of this tumor is difficult, that in the second case being made only on operation for dacryostenosis. These 2 cases occurred within a very short time, and a little later a third case was seen, which in view of the other cases was especially interesting. The growth, in this case, however, proved to be a granuloma due to a chronic inflammatory process. The result of the study of these cases emphasized the importance of completely removing the lacrimal sac at operation, leaving nothing in place and destroying as fully as possible the mucous membrane in the lacrimal canal. They also emphasize the importance of histologic examination of the tissue removed.

S B MARLOW

PLEXIFORM NEUROMA OF THE LACRIMAL CARUNCLE AND CILIARY BORDER M BIRCH BARRAQUER, Arch Soc oftal hispano-am 4: 245 (April) 1945

A unique case of this condition is reported. A man aged 51 had noticed ten years before a small tumefaction in each caruncle. At the time of examination a smooth, round, pink tissue formation, about the size of a small pea, was present at the site of each caruncle, preventing the proper approximation of the lids and producing considerable epiphora. Besides, another small, regular growth was observed at the ciliary margin of each lower lid about 4 mm from the outer canthus. These tumors were excised and examined microscopically. They showed the characteristic histopathologic picture of plexiform neuromas. The author states that this report is the only record in the literature of a similar tumor in this location. Numerous photographs and photomicrographs are shown in the article.

H F CARRASQUILLO

LOCALIZATION OF INTRACRANIAL AND ORBITAL DERMoids H KRAYENBUHL and A E SCHMID, Ophthalmologica 106: 25 (May-June) 1943

A woman aged 23 had progressively increasing unilateral exophthalmos, due to a dermoid, of hourglass shape, which extended into the middle fossa of the skull and the zygomatic temporal fossa. The differential diagnosis of orbital dermoids is discussed, and the surgical method of approach is described.

F H ADLER

Uvea

TRAUMATIC ARCIFORM CHOROIDITIS HUDELO, GUILLAUMAT and MAUSSION, Arch d'opht 5: 44, 1945

The authors present 4 observations on this condition, in 2 of which the so-called rupture of the choroid was not evident for a time after the injury. The clinical picture and the mechanism by which the process occurs are discussed. The authors propose the hypothesis that the lesion is not really a tear but, rather, represents traumatic necrosis of the choroid, perhaps trophic in nature. The arguments which support their hypothesis are the absence of the rupture in the beginning, the total absence of edema and the absence of hemorrhage.

S B MARLOW

PRIMARY ATROPHY OF THE IRIS REPORT OF A CASE H ARRUGA,
Arch Soc oftal hispano-am 4. 233 (April) 1945

Airuga reports a case of this rare condition in a woman aged 25. Besides the normal pupillary opening in the right eye, which was displaced up and to the right, there were three other openings in the iris, extending from the periphery to near the margin of the pupil. The fundus could be seen through these holes. The condition had begun two years before and had gradually extended. The eye was otherwise normal. This is the only case observed by the author, and he notes that he could find only 3 cases in the literature, reported by Zentmayer, de Schweinitz and Arnold. The article is illustrated.

H F CARRASQUILLO

Vision

A VISUAL TEST FOR INFANTS J N EVANS, Am J Ophth 29:73
(Jan) 1946

Evans suggests the use of a series of sizes of iron filings moved by a magnet under the tray to determine an infant's vision.

W S REESE

DIMINUTION OF VISION IN RETURNED PRISONERS OF WAR (CORRESPONDENCE) D FITZGERALD MOORE, Brit M J 2:400 (Sept 22) 1945

Many of those who have been prisoners of war in Japanese hands have returned with the following symptoms: sore throat, cracked lips, dry skin, scaly scrotum, various nervous manifestations and, particularly, retrobulbar neuritis, which if left untreated went on to partial atrophy of the optic nerve of varying severity. From the author's experience in West Africa, where he observed this condition in the years from 1930 to 1938, particularly with regard to impaired vision, he has come to the following conclusions:

It was worth while to treat all patients having a history up to twelve months. Over that period, improvement was problematic unless the symptoms of malnutrition were still present. When the diminution of vision had not existed longer than a year, the prognosis was good, while for those who had had it six months or less it was excellent. Even in the patients who were cured asthenopic symptoms were apt to persist, and the most important symptom was photophobia. The author treated these patients with 1 ounce (31 Gm) a day of Marmite (extract of yeast containing the vitamin B complex) for at least six months. The condition of the eye began to show improvement after a period of three to six weeks, while in some cases in which the irreversible stage had been reached no improvement occurred, though persistence in treatment was always justified. In Nigeria these symptoms were prevalent during the old government boarding school days. None of these patients became blind, but the condition remained practically stationary, in contradistinction to the progressive changes occurring with primary atrophy of the optic nerve. Absolute blindness does not occur though the vision may be very much reduced, even to perception of hand movements only.

The lesions of the mouth and skin cleared up rapidly. There is no question that a riboflavin deficiency played a major part, though probably other factors of the vitamin B complex were involved. Hence it would be wise in the general treatment to include the whole of the vitamin B complex. Brewer's yeast was not liked, while Marmite seems to have been exceedingly well taken by Africans. It is essential to regard a higher nutritional diet for these patients as an integral part of the treatment. It was quite natural that these symptoms would also become manifest under the conditions in which prisoners of war have lived in Japan. The dietary was very similar to the one in West Africa, namely, rice, manioc, occasionally sweet potatoes, a little fish, some green food and red palm oil.

ARNOLD KNAPP

Sympathetic Ophthalmia

EARLY DIAGNOSIS OF SYMPATHETIC OPHTHALMIA X BULACH,
Vestnik oftal 23:7, 1944

In an attempt to find early diagnostic signs of sympathetic ophthalmia, Bulach examined the blood of all patients with perforating injuries of the eye. He examined 335 patients with such injuries during 1943, 120 eyes were enucleated. Of these eyes, the process in 3 was diagnosed as sympathetic ophthalmia on pathologic examination.

An increased monocyte count was found as a rule in cases of serious bilateral iridocyclitis, panophthalmitis and endophthalmitis. There was a normal monocyte count in cases of low grade uveitis, as well as in the 3 cases of verified sympathetic iridocyclitis. Bulach, therefore, does not consider monocytosis to be of value in the diagnosis of sympathetic ophthalmia.

O SITCHEVSKA

Therapeutics

SUB-CONJUNCTIVAL PENICILLIN AND INTRA-OCULAR INFECTION.
B W RYCROFT, Brit J Ophth 29:501 (Oct) 1945

From a survey of the experimental evidence in the literature, Rycroft believes that certain conclusions can be reached so far as rabbits are concerned.

Direct intravitreous injections of penicillin constitute the most effective means of obtaining high concentrations and bacteriostasis in the vitreous. A single injection of purified penicillin does little harm and will control susceptible infection if given within twelve hours and will maintain bacteriostasis up to at least twenty-four hours. Multiple injections cause serious intraocular damage. Local application of drops or ointment will not result in the penetration of penicillin into the aqueous in normal eyes but will do so when the cornea is inflamed or traumatized. Iontophoresis, constant corneal baths and subconjunctival injections will maintain bacteriostatic levels in the aqueous, especially in the presence of inflammation. Intramuscular and intravitreous injections of penicillin do not produce bacteriostatic levels in the aqueous or vitreous and will not control experimental susceptible inflammation there.

It was decided to determine the value of subconjunctival injections in the treatment of intraocular infection in man. The eyes selected

either were hopelessly blind and due for removal or required conservative operation. After subconjunctival injections of 4,000 Oxford units of penicillin, the drug penetrated to the aqueous humor in 7 of the 8 cases after an interval of fifteen minutes. Failure to reach the aqueous in the one case was probably due to the short interval of aspiration after injection. Assay of the vitreous was carried out in 6 cases in 3 of which bacteriostasis appeared in forty-five minutes. The other 2 or 3 eyes were examined thirty minutes or less after injection, and this may account for the lack of inhibition. All amounts of penicillin detected in the aqueous or vitreous were above the bacteriostatic level.

Rycroft reaches the following conclusions:

Subconjunctival injection of sodium penicillin equivalent to 4,000 Oxford units will produce bacteriostasis of susceptible organisms in the aqueous humor of the human eye within one-half hour of injection. It is probable that the same state of affairs is later attained in the vitreous humor and is likely to remain for at least twenty-four hours.

Subconjunctival injections of penicillin represent a practical method by which penicillin may reach the interior of the eye. They have been widely employed without harmful effects, and the earlier they are employed the better the results.

Large doses should be employed not only because of the slow rate of diffusion but to avoid the risk of producing resistance to penicillin.

Florey has written, "Penicillin must be kept continuously in contact with all infected tissues until the natural body defenses have had time to deal with the infection." It is therefore probable that the best results of penicillin therapy for deep intraocular infection will be obtained by a combination of routes, and of these the subconjunctival is practicable and harmless. Experimental evidence stresses the importance of bringing the drug in contact with the invading organism at the earliest possible stage.

W ZENTMAYER

PENICILLIN IN OPHTHALMOLOGY. AN INTERIM REVIEW. A. SORSBY,
Brit J Ophth 29 511 (Oct) 1945

After a survey of the experimental and clinical data concerning the use of penicillin in ophthalmology, Sorsby relates his personal clinical experience. In his discussion he states that it would seem that the dosage must be determined by the causal organism rather than by the patient's tolerance. When applied in the form of drops a solution of the substance in a concentration of 2,500 units per cubic centimeter seems to be safe and in most cases adequate. For direct injection into the anterior chamber it seems for the present that 200 units in 0.25 cc is as much as it is justifiable to give. When the drug is injected into the vitreous, it is doubtful whether it is justifiable to give more than 100 units, or even as much. Pending further clarification, subconjunctival injection seems to be the method of choice for intraocular infection, though experimental evidence does not indicate that this is a particularly satisfactory method of obtaining an adequate concentration in the interior of the eye.

W ZENTMAYER

PSYCHO-THERAPY IN HYSTERICAL AMBLYOPIA P D GIRIDHAR,
Indian J Ophth 6:32 (July) 1945

Giridhar stresses that hysterical amblyopia is in fact a psychopathic disease in which the patient forgets that he can see and vision is said to be lost, but that when the patient is convinced that he can actually see he indeed begins to see. The disease is mental rather than physical, and the apparent loss of vision can be restored by a tactful and psychic handling of the patient.

Four cases are recorded, in all of which vision was restored by suggestion and by subconjunctival injections of saline solutions.

W ZENTMAYER

LOCAL USES OF PENICILLIN IN OPHTHALMOLOGY K KRISHNAMURTY,
Indian J Ophth 6:34 (July) 1945

In this article Krishnamurty deals with the local use of penicillin only. Penicillin in the form of an ointment has been found superior to powder or drops. The ointment should be applied six times daily. In cases of conjunctivitis clinical cure occurs within forty-eight hours. In cases of trachoma, redness, watering of the eyes, blepharospasm and photophobia disappear in the first week, and in the second week the granules begin to flatten. In the third week the process of scarring appears.

W ZENTMAYER

Toxic Amblyopia

SEVERE AMAUROSIS DUE TO QUININE POISONING REPORT OF A CASE
R ANTOINE, R LEGROUS and P STRICKER, Arch d'opht 5:349,
1945

The authors describe a case of amaurosis due to quinine poisoning which came on rapidly, with marked constriction of the fields of vision. Their purpose in presenting the case is to demonstrate the beneficial action of acetylcholine. The rapid improvement occurred after four infiltrations into the superior cervical sympathetic ganglion. The fields of vision were not reestablished spontaneously but were restored to normal only on repeated treatment of the sympathetic ganglion. The first return of vision was the perception of light, and then vision was restored in the temporal field. The authors discuss the distribution of the blood supply of the optic nerve and the chiasm in relation to this condition. The intermingling of the sympathetic fibers is an important consideration in treatment with the vasodilator drugs.

S B MARLOW

Book Reviews

Cirugía ocular By H Arruga Pp 888 Barcelona, Spain Salvat Editors, S A , 1946 Price 380 pesos

The author, well known in Europe and the Continent for his skill as an ophthalmic surgeon, has brought together in this volume the fruits of his wide knowledge and experience. This book is essentially a practical treatise, in which Arruga gives credit to the numerous writers whose methods he describes. A number of his own ingenious instruments and surgical procedures are presented.

After a chapter dealing with the general principles of ocular surgery, Arruga, in a systematic fashion, treats of the surgery of the eyelids, lacrimal apparatus, conjunctiva, cornea, sclera, iris, ciliary body and choroid, lens, extraocular muscles, eyeball, vitreous and orbit and the operative treatment of detachment of the retina, glaucoma and intraocular foreign bodies. The chapters dealing with the lacrimal passages, cataract extraction and detachment of the retina are outstanding, in the opinion of the reviewer, but the remaining sections are valuable.

It is only to be expected that some American ophthalmologists will not agree with all of Arruga's statements. For example, the author, in his chapter on the extraocular muscles, does not favor tenotomy or myectomy of the inferior oblique muscle by way of an incision in the inferior conjunctival cul-de-sac, nor does he recommend any operative procedure on this muscle at its insertion into the globe.

The book is beautifully printed and contains 1,218 illustrations, of which 119 are in color. In the excellence and clarity of the drawings, this volume is a superb contribution to the world's ophthalmologic literature. It is to be hoped that the author will arrange for an English translation, and thus further cement the friendly bonds which link ophthalmologists in this country with their Spanish-speaking colleagues.

CHARLES A PERERA, M D

INTRAOCULAR HEMORRHAGE IN CATARACT EXTRACTION

WILLIAM COUNCILMAN OWENS, M D

AND

WILLIAM F HUGHES Jr, M D

BALTIMORE

THE LITERATURE on intraocular hemorrhage associated with cataract extraction has been reviewed at length by various authors, and the possible causes of this complication have been widely discussed¹ The majority of the reports lack sufficient data to permit a statistical analysis of etiologic factors and adequate deduction of prophylactic measures Therefore, we have reviewed the material which formed the basis of our former report²—i e, 2,086 extractions of uncomplicated senile cataract performed at the Wilmer Ophthalmological Institute

From the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital and University

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, March 18, 1946

1 (a) DeVoe, G Hemorrhage After Cataract Extraction, *Arch Ophth* 28.1069 (Dec) 1942 (bibliography before 1943) (b) Broman, T On the Occurrence of Iritis After the Extraction of a Cataract, *Acta ophth* 14.170, 1936 (c) Purtscher, E, and Dibold, H Zur intrakapsularen Starextraktion beim Diabetiker, *Klin Monatsbl f Augenh* 98.24, 1937 (d) Meyer, F W Ueber die postoperative Nachblutung nach Starextraktion und ihre Ursachen, *ibid* 102: 479, 1939 (e) Kotz, H Nachblutungen nach Altersstaroperationen, *ibid* 108 291, 1942 (f) Gradle, H S, and Sugar, H S Wound Rupture After Cataract Extraction, *Am J Ophth* 25 426, 1942 (g) Klein, M Operation for Cataract, *Brit J Ophth* 26 93, 1942 (h) McArevey, J B Postoperative Hemorrhages, *Tr Ophth Soc U Kingdom* 63.407, 1943 (i) Davis, F A Intracapsular Cataract Extraction, *Arch Ophth* 31.367 (May) 1944 (j) Kirby, D B Further Experiences with a System of Intracapsular Extraction of Cataract, *ibid* 31 302 (April) 1944 (k) Dunnington, J H Some Complications of Cataract Extraction, *New York State J Med* 44 2224, 1944 (l) Mathewson, W R Vitamin P in Ophthalmology, *Brit J Ophth* 28.336, 1944 (m) Mann, I Effect of Ascorbic Acid on the Occurrence of Hyphema After Cataract Extraction, *ibid* 29.175, 1945 (n) Neff, E Factors Affecting Hemorrhage Following Cataract Extraction, *Arch Ophth* 33 192 (March) 1945 (o) Atkinson, W S Preliminary Report of Corneal Section with Long Bevel and Conjunctival Flap for Cataract Extraction, *Tr Am Ophth Soc* 43 97, 1945

2 Hughes, W F, Jr, and Owens, W C The Extraction of Senile Cataract A Statistical Comparison of Various Techniques and the Importance of Preoperative Survey, *Am J Ophth* 28.40, 1945

between November 1925 and October 1943—for any information it might yield on ocular hemorrhage. The results are analyzed statistically, and no factor is considered significant unless the probability of chance is less than 1 in 20 ($p = 0.05$).

In the study of this problem, we have asked ourselves the following questions: 1. What factors in the patient's physical status or in the operative technic produce intraocular hemorrhage? 2. How may these factors be controlled or altered to prevent this complication? 3. What effect does each type of hemorrhage have on the postoperative course and the final visual results?

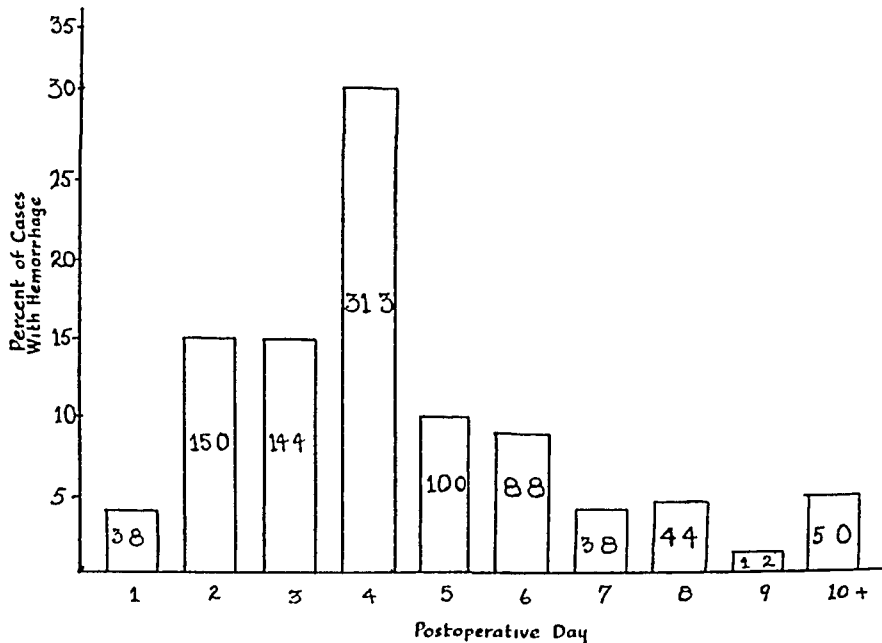


Chart 1—Onset of postoperative hemorrhage into the anterior chamber

Three types of intraocular hemorrhage are evaluated in this study: (1) postoperative hemorrhage into the anterior chamber, (2) hemorrhage into the anterior chamber occurring at the time of operation and (3) expulsive, or subchoroidal, hemorrhage.

POSTOPERATIVE HEMORRHAGE INTO THE ANTERIOR CHAMBER

Incidence—Differences in the reported incidence of postoperative hemorrhage into the anterior chamber are probably due to variations in definition. In this study, fresh bleeding seen at the time of the first dressing or at subsequent dressings was defined as postoperative hemorrhage into the anterior chamber. Flecks of blood occasionally noted at the first dressing were probably residua of hemorrhage at the time of operation and were not considered postoperative hemorrhage. Postoperative hemorrhage occurred in 195 cases (9.3 per cent). In 71 of

these (36 per cent) the hemorrhages were designated as "severe" because they either filled the anterior chamber completely or were recurrent

Time of Onset—In this series, the usual period for the occurrence of postoperative hemorrhage into the anterior chamber was between the second and the sixth day after operation (chart 1) This is in accord with the figures of other reports

Duration—The blood was completely absorbed from the anterior chamber during the first seven days after the appearance of the hemorrhage in 78.9 per cent of the cases with mild hemorrhage but in only 43.3 per cent of the cases with severe hemorrhage (chart 2)

TABLE 1—*Effect of Age on Postoperative Hemorrhage into Anterior Chamber*

Age, Yr	No. of Cases	Postoperative Hemorrhage into Anterior Chamber, per Cent
Less than 50	211	11.4
50 to 59	475	11.6
60 to 69	760	9.2
70 to 79	547	8.1
Over 80	91	9.9

SYSTEMIC FACTORS PRODUCING POSTOPERATIVE HEMORRHAGE INTO THE ANTERIOR CHAMBER

In order to determine what factors in the patient's general physical status might predispose to the occurrence of postoperative hemorrhage into the anterior chamber, the cases were analyzed from the following standpoints (1) age, (2) blood pressure, (3) blood-clotting mechanisms, (4) diabetes, (5) syphilis and (6) foci of infection

Age—The age of the patient had no relation to the occurrence of postoperative hemorrhage into the anterior chamber (table 1)

TABLE 2—*Effect of Blood Pressure on Postoperative Hemorrhage into Anterior Chamber*

Systolic Blood Pressure, Mm Hg	No. of Cases	Postoperative Hemorrhage into Anterior Chamber, per Cent	Diastolic Blood Pressure, Mm Hg	No. of Cases	Postoperative Hemorrhage into Anterior Chamber, per Cent
Less than 120	164	11.0	Less than 70	128	9.4
120 to 139	457	8.3	70 to 79	381	9.6
140 to 159	559	10.4	80 to 89	641	10.6
160 to 179	369	8.4	90 to 99	496	9.7
180 to 199	294	9.8	100 to 109	223	4.5
200 to 219	136	11.8	Over 110	185	11.9
Over 220	75	10.4			

Blood Pressure—Hypertension has been considered an important cause of postoperative hemorrhage into the anterior chamber In this series, the occurrence of postoperative hemorrhage was completely independent of the patient's systolic or diastolic blood pressure In patients with systolic pressure of from 120 to over 200 mm of mercury, the

percentage of occurrence varied only from 8.3 to 11.8. In patients with diastolic pressure of from 70 to over 110 mm of mercury, the percentage of occurrence was between 4.5 and 11.9, the low incidence occurring in patients with a diastolic pressure of 100 to 109 mm (table 2)

Blood-Clotting Mechanism—A low prothrombin level has been considered a cause of hemorrhage into the anterior chamber, although Quick³ and others have shown that 80 per cent of the serum prothrombin can be lost before the coagulation time is appreciably prolonged and a hemorrhagic tendency develops. Foss, DeVoe and Davis⁴ found no relation between the occurrence of postoperative hemorrhage and the

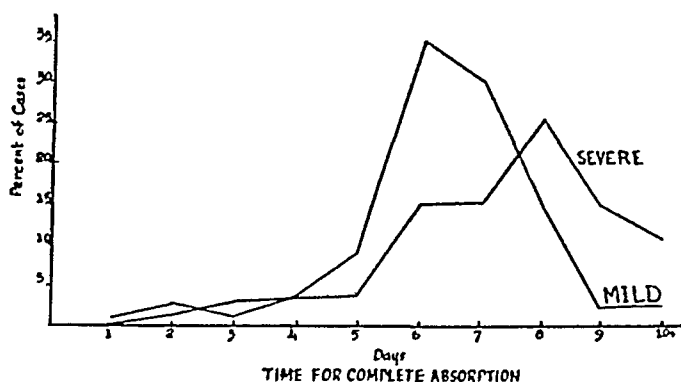


Chart 2—Duration of postoperative hemorrhage into the anterior chamber

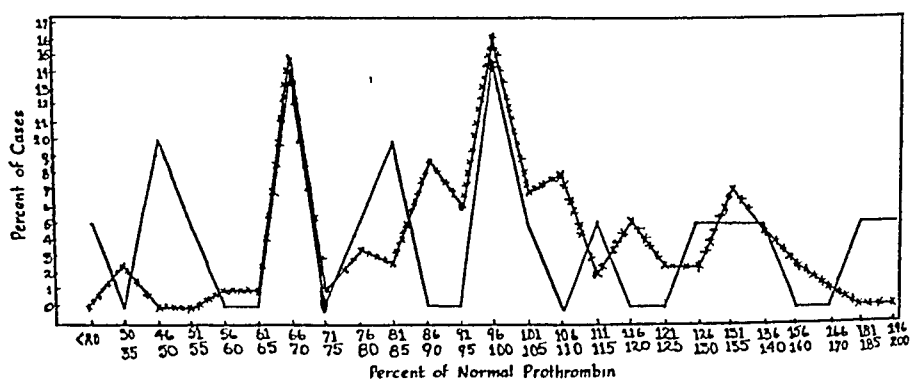


Chart 3—Relation of prothrombin levels to postoperative hemorrhage into the anterior chamber. Values for the cases with hemorrhage are indicated by the solid line, values for the cases without hemorrhage, by the line with crosses.

plasma prothrombin level. In 133 of our cases in which the plasma prothrombin level was determined by the method of Warner, Brinkhous and Smith⁵ no significant relationship was found between the pro-

3 Quick, A. J. A Classification of Hemorrhagic Disease Due to Defects in the Coagulation Mechanism of the Blood, *Am J M Sc* **199** 118, 1940.

4 Foss, B. Gibt es eine K-Vitamininsuffizienz bei Blutungen nach intrabulbaren Eingriffen? *Acta ophth* **19** 15, 1941. DeVoe^{1a} Davis¹¹

5 Warner, E. D., Brinkhous, K. M., and Smith, H. P. A Quantitative Study on Blood Clotting. Prothrombin Fluctuations Under Experimental Conditions, *Am J Physiol* **114** 667, 1936.

thrombin levels and postoperative hemorrhage (chart 3) In only 1 case was the prothrombin level less than 20 per cent of normal, which Quick has stated as the critical level In this case a severe postoperative hemorrhage occurred However, when a cataract extraction was performed on this patient's other eye one year later, the prothrombin level was 99 per cent of normal, and the patient had been under prophylactic treatment with vitamin K In spite of this, the second operation was followed by a severe hemorrhage

TABLE 3—*Effect of Severity of Diabetes on Severe Postoperative Hemorrhage into Anterior Chamber*

Severity of Diabetes	No of Cases	Severe Hemorrhage into Anterior Chamber, per Cent
Duration less than 9 yr	166	18
Duration 9 yr or more	58	10.4
Insulin per day less than 30 units	169	18
Insulin per day 30 units or more	55	10.9
Duration 9 yr or more and insulin per day 30 units or more	19	21.0

The clotting time was measured by the standard tube method in 50 cases with postoperative hemorrhage into the anterior chamber and in 46 cases without postoperative hemorrhage In all these cases the clotting time was less than fifteen minutes, the upper limit of normal with this method

Diabetes—Postoperative hemorrhage into the anterior chamber occurred in 12.4 per cent of 235 cases with diabetes and in 9.2 per cent of 1,852 cases without diabetes Although suggestive of a correlation between the presence of diabetes and hemorrhage, this over-all observed

TABLE 4—*Effect of Blood Sugar Level on Postoperative Hemorrhage into Anterior Chamber*

Highest Preoperative or Postoperative Blood Sugar	No of Cases	Postoperative Hemorrhage into Anterior Chamber, per Cent
Less than 175 mg /100 cc	159	13.2
Over 175 mg /100 cc	63	8.0

difference is not statistically significant However, patients with diabetes of long standing, or those requiring large amounts of insulin, showed an increased incidence of severe hemorrhage, the incidence rising sharply to 21 per cent in patients with diabetes of over nine years' duration and requiring over 30 units of insulin per day for regulation (table 3) It is interesting that there was no similar relationship between mild postoperative hemorrhage and the duration or severity of diabetes

There was no significant relationship between the preoperative or postoperative blood sugar level and the occurrence of postoperative

hemorrhage (table 4) Likewise, the diabetic patients with central retinitis had essentially the same incidence of postoperative hemorrhage as those without central retinitis (table 5)

Syphilis—In this series, there were 64 cases of late latent syphilis with positive serologic reactions and 41 cases of late visceral or neuro-

TABLE 5—*Relation of Central Retinitis in Diabetic Patients to Postoperative Hemorrhage into Anterior Chamber*

Central Retinitis	No of Patients	Postoperative Hemorrhage into Anterior Chamber, per Cent
Present	43	11.6
Absent	189	12.7

syphilis Table 6 shows that the incidence of postoperative hemorrhage into the anterior chamber was essentially the same in the syphilitic patients as in the nonsyphilitic patients

Foci of Infection—A thorough preoperative search for foci of infection was made on 1,482 patients It included a general physical exam-

TABLE 6—*Effect of Syphilis on Postoperative Hemorrhage into Anterior Chamber*

Syphilis	No of Cases	Postoperative Hemorrhage into Anterior Chamber, per Cent
Present	105	10.5
Absent	1,917	9.7

ination, routine consultation with an otolaryngologist (usually including roentgenologic studies of the sinuses), dental consultation with roentgenographic studies, consultation with the gynecologic or urologic departments if indicated, a Wassermann test of the blood, urinalysis and often

TABLE 7—*Effect of Focus of Infection on Postoperative Hemorrhage into Anterior Chamber*

Focus	No of Cases	Postoperative Hemorrhage into Anterior Chamber, per Cent
Present inadequate treatment	188	10.7
Present adequate treatment	188	10.1
Absent	1,106	9.8

tuberculin sensitivity tests and roentgenologic examination of the chest As a result of this study, 1,106 patients were found free of foci, but definite foci were found in 376 patients Half the latter group received adequate treatment of the focus before the cataract extraction The presence or absence of a focus of infection had no relation to the occurrence of postoperative hemorrhage into the anterior chamber (table 7)

FACTORS IN OPERATIVE TECHNIC

An analysis was made of the following factors in the operative technic which might influence the occurrence of postoperative hemorrhage into the anterior chamber (1) type of cataract extraction, (2) type of operation on the iris, (3) use of sutures and (4) loss of vitreous

Type of Cataract Extraction—The cases were divided into three groups, according to the type of extraction (1) intentional extracapsular

TABLE 8—*Effect of Type of Extraction on Postoperative Hemorrhage into Anterior Chamber*

Type of Extraction	No of Cases	Postoperative Hemorrhage into Anterior Chamber, per Cent
Extracapsular	639	8.8
Broken capsule	335	11.9
Intracapsular	1,011	9.3

extraction, (2) attempted intracapsular extraction in which the capsule ruptured during the operation and (3) intracapsular extraction. The observed differences in the occurrence of hemorrhage in these three groups were not large enough to be significant, varying only between 8.8 and 11.9 per cent (table 8)

Use of Sutures—Four types of closure of the operative wound were used: no sutures, sutures in a pocket conjunctival flap and one or two

TABLE 9—*Influence of Sutures on Postoperative Hemorrhage into Anterior Chamber*

Sutures	No of Cases	Hemorrhage into Anterior Chamber, per Cent
None	390	7.7
Conjunctival	629	12.2
Corneoscleral (one)	482	13.3
Corneoscleral (two)	558	4.7

corneoscleral sutures. As may be seen from table 9, the use of two corneoscleral sutures to secure firm closure of the wound decreased the incidence of postoperative hemorrhage. However, the cases without sutures and relatively shallow sections also had a low incidence of postoperative hemorrhage. The shallow sections in this group probably healed with little vascularization. Thus, the ideal section for the reduction of postoperative hemorrhage into the anterior chamber seems to be a shallow one firmly closed with two corneoscleral sutures.

Type of Operation on the Iris—The cases were divided into groups according to the type of suture used and then subdivided according to the type of operation on the iris. In all groups—those without sutures, those with conjunctival sutures or those with one and two corneoscleral sutures—there was a slight increase in postoperative

hemorrhage when a full iridectomy was performed at the time of operation (table 10). However, this difference was not statistically significant.

Loss of Vitreous—There was a progressive increase in the incidence of postoperative hemorrhage into the anterior chamber with the loss of increasing amounts of vitreous. The percentage incidence of hemorrhage into the anterior chamber rose from 8.9 in cases without loss of vitreous to 23.9 in cases in which there had been a great loss of vitreous (table 11).

TABLE 10—*Influence of Sutures and Type of Iridectomy on Postoperative Hemorrhage into Anterior Chamber*

Sutures	Iridectomy	No of Cases	Hemorrhage, per Cent
None	Full	280	8.1
	Preliminary	107	6.6
Conjunctival	Full	523	14.0
	Preliminary	103	10.7
One corneoscleral	Full	426	14.3
	Round pupil	40	7.5
Two corneoscleral	Full	179	6.1
	Round pupil	374	4.0

TABLE 11—*Effect of Loss of Vitreous on Postoperative Hemorrhage into Anterior Chamber*

Loss of Vitreous	No of Cases	Postoperative Hemorrhage into Anterior Chamber, per Cent
None	1,720	8.9
Presentation	154	9.8
Moderate	141	12.0
Severe	46	23.9

TABLE 12—*Relation of Other Complications to Postoperative Hemorrhage into Anterior Chamber*

Postoperative Hemorrhage into Anterior Chamber	No of Cases	Incomplete Closure of Wound, per Cent	Delayed Reformation of Anterior Chamber, per Cent	Prolapse of Iris, per Cent	Iridocyclitis, per Cent
Present	195	3.6	1.0	3.6	4.6
Absent	1,891	2.8	1.1	3.3	6.3

OTHER FACTORS

Hemorrhage into the anterior chamber followed the removal of corneoscleral sutures in 3.6 per cent of the cases in which they were used. However, these hemorrhages were mild, cleared uneventfully and had no effect on the final visual results.

No relationship was found between postoperative hemorrhage and visible gaping of the wound, delayed reformation of the anterior chamber, prolapse of the iris or iridocyclitis (table 12).

SUMMARY OF CAUSES OF HEMORRHAGE INTO
ANTERIOR CHAMBER

The data given previously have shown that, except for severe diabetes, the general systemic condition of the patient is unrelated to the occurrence of postoperative hemorrhage. So far as operative technic is concerned, the use of two corneoscleral sutures to close the wound more securely was found to be an important factor in reducing the incidence of this complication. Since hemorrhages into the anterior chamber occur most frequently between the second and the sixth postoperative day and are less common in eyes with shallow sections, it is a logical deduction that postoperative hemorrhage results from a rupture of the small capillaries that have grown into the healing incision. In many cases the blood can be seen to arise from the section and trickle into the anterior chamber immediately after minor trauma or after removal of the corneoscleral sutures. When the sutures are deeply placed or the patient is uncooperative, hemorrhage can be prevented by postponing the removal of sutures until the wound is more securely healed. The increased incidence of hemorrhage after loss of vitreous can be attributed to the poor healing of the wound in such cases.

VISUAL RESULTS

The visual results were significantly poorer in the cases of postoperative hemorrhage into the anterior chamber. Table 13 shows that in only 67 per cent of the cases with postoperative hemorrhage was there a visual result of 20/30 or better, while in 81 per cent of the cases with-

TABLE 13—*Effect of Postoperative Hemorrhage into Anterior Chamber on Visual Result*

Postoperative Hemorrhage into Anterior Chamber	No. of Cases	Visual Results, per Cent		
		20/15 to 20/30	20/40 to 20/70	20/100 or Less
Present	143	67.0	15.4	17.5
Absent	1,336	81.5	8.7	9.9

out hemorrhage there was a visual result of 20/30 or better. This tabulation includes only those cases in which an adequate refraction had been made and in which there were no causes of poor vision independent of the cataract extraction, such as senile macular degeneration. The major cause of the poor results after hemorrhage was found to be persistent opacities in the vitreous. Such opacities were the primary cause of reduction of vision below 20/30 in 20.2 per cent of the cases in which postoperative hemorrhage occurred, in contrast to 12.2 per cent of cases without hemorrhage. In many of the cases with postoperative hemorrhage into the anterior chamber, a reduction or abolition of the red reflex persisted after absorption of the blood from the anterior chamber. This

was probably due to a seepage of blood into the vitreous, where further absorption proceeded slowly and often resulted in persistent opacities in the vitreous. In a few cases blood could be seen in the vitreous in spite of an intact hyaloid membrane.

In some cases with severe hemorrhage into the anterior chamber a membrane persisted over the pupillary space. Even after intracapsular

TABLE 14—*Relation of Postoperative Hemorrhage into Anterior Chamber to Glaucoma and Phthisis Bulbi*

Postoperative Hemorrhage into Anterior Chamber	No of Cases	Postoperative Glaucoma, per Cent	Phthisis Bulbi, per Cent
Present	195	5.6	2.6
Absent	1,591	4.3	1.3

extractions, a discussion was occasionally necessary. After extracapsular extractions, blood lying on the posterior capsule is absorbed extremely slowly and frequently results in a thick pupillary membrane.

Postoperative hemorrhage did not predispose to late secondary glaucoma or phthisis bulbi (table 14).

HEMORRHAGE INTO THE ANTERIOR CHAMBER OCCURRING AT OPERATION

There were 36 cases in this series in which blood remained in the anterior chamber at the end of operation because of unusually severe bleeding. This occurred more frequently in older patients (table 15).

TABLE 15—*Effect of Age on Operative Hemorrhage into Anterior Chamber*

Age, yr	No of Cases	Operative Hemorrhage into Anterior Chamber, per Cent
Less than 60	686	0.9
60 to 69	769	1.6
70 or over	638	2.8

and in patients in whom the sections were deeply placed. No other factors were found to have any relationship to hemorrhages at operation. The hemorrhages occurring at operation were absorbed rapidly and had no effect on the final visual result.

EXPULSIVE HEMORRHAGE

In 18,866 cases of cataract extraction reported in the literature, the incidence of expulsive hemorrhage was 0.3 per cent.⁶ Three such

6 de Wecker, cited by Ziegler, L. S. The Problem of Choroidal Hemorrhage in Cataract Extraction, in Contributions to Ophthalmic Science, Menasha, Wis.

(Footnote continued on next page)

hemorrhages occurred in our series, 1 at the time of operation, another a few hours after operation and the last on the third postoperative day. Although expulsive hemorrhages have been reported to occur in patients as young as 25 years of age, all 3 patients in our series were over 70. Contrary to the general opinion, the blood pressure is usually normal. Of 15 reported cases in which the blood pressure was stated, the systolic pressure was greater than 140 mm of mercury in only 5, the highest being 180 mm. In only 2 of these was the diastolic pressure above 90 mm. The blood pressures of our 3 patients were 115 systolic and 70 diastolic, 142 systolic and 76 diastolic and 210 systolic and 110 diastolic.

CONCLUSIONS

A statistical analysis is presented of all the cases of hemorrhage occurring in 2,086 extractions of uncomplicated senile cataract. Except for severe diabetes, the general systemic condition of the patient is unrelated to postoperative hemorrhage into the anterior chamber. Operative technics promoting firm closure and avascular healing of the incision reduced the incidence of this complication. These technics include the use of two corneoscleral sutures and a shallow section. The visual results were significantly poorer in the cases with postoperative hemorrhage into the anterior chamber than in the cases without hemorrhage. This was chiefly due to persistent opacities in the vitreous.

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EFFECT OF TRAINING METHODS ON COLOR VISION

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IN VARIOUS surveys it has been found that from 6 to 8 per cent of unselected males are unable to make the proper responses to a series of color vision test plates¹. At the present time certain specialized branches of the armed services require that applicants be able to read correctly all the series of these plates, consequently, a number sufficiently large to make color vision testing a matter of considerable significance could be rejected. In a recent publication^{1b} the efficiency of some of the plates used in one testing method was questioned, and the suggestion was made that only a small number (ten) of these plates need be used for the satisfactory evaluation of color vision². In that publication² these ten plates are referred to as "key" plates. Regardless of the reliability of various testing methods or the desirability of altering present standards, there still remains the problem whether the color vision of those who fail to pass these tests can be modified. Whenever large numbers of persons are excluded either from a branch of the armed services or from a civilian occupation because of a physical disability, there will develop a demand from those affected that the disability be remedied or that the standards applying to it be lowered. In the problem at hand, the rejection of many otherwise well qualified men has led to efforts to

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1 (a) Miles, W R. Color Blindness in Eleven Thousand Museum Visitors, *Yale J Biol & Med* **16** 59-76 (Oct.) 1943. (b) Gallagher, J R., Gallagher, C D, and Sloane, A E. A Critical Evaluation of Pseudo-Isochromatic Plates and Suggestions for Testing Color Vision, *ibid* **15** 79-98 (Oct.) 1942. (c) Judd, D B. Facts of Color Blindness, *J Optic Soc America* **33** 294-307 (June) 1943.

2 Gallagher, J R., Gallagher, C D, and Sloane, A E. A Brief Method of Testing Color Vision with Pseudo-Isochromatic Plates, *Am J Ophth* **26** 178-181 (Feb.) 1943.

improve the color vision of these rejectees so that subsequently they might be able to pass the color vision tests. These efforts have been considered in the light of rehabilitation, inasmuch as it was believed that many applicants failed these tests because of color ignorance, a condition which would obviously be more amenable to treatment than one attributable to a disorder of any physiologic aspect of color perception. However, it is of great importance to know whether such training methods improve the subject's color perception in all situations or whether they only enhance his ability to pass a specific test by improving, at the cerebral level, his ability to interpret that particular test. If the latter is true, the employment of such training methods may be highly undesirable, and the retention of a testing method the results of which can be modified by such procedures would seem questionable. An excellent discussion of the effect of various training methods on visual functions has recently been published by Lancaster³. In an effort to determine the effect of training methods, a group of subjects previously identified as being deficient in color vision was studied.

I TRAINING ON AMERICAN OPTICAL COMPANY PLATES

Method—All 701 students at a boys' preparatory school were given a color vision test, using 10 of the American Optical Company's Pseudo-Isochromatic Plates⁴. From this group of 701 subjects, 49 (6.9 per cent) were judged to have deficient color vision, an indication that this group was a normal sample. Those whose color vision was deficient were subsequently retested, at which time 46 plates in that pseudoisochromatic series were used. In table 1 the distribution

TABLE 1—*Distribution of Both Number of "Key" Plates Failed in Initial Test and Number of Plates Failed When the Entire Series of Plates (46) Was Given **

No of Subjects	No of "Key" American Optical Company Plates Failed	No of Subjects	No of American Optical Company Plates in Entire Series (46) Failed
2	1	6	8 - 13
2	2	9	18 - 24
6	3	10	25 - 30
3	4	14	31 - 36
8	5	6	36 - 41
7	6	0	42 - 46
8	7		
9	8		

* These 45 subjects, out of the group of 701 who were classified as being deficient in color vision, were later given training, 4 others whose training was not carried to completion are not included in this table.

of the number of key plates and the number of total plates to which the incorrect response was given are recorded. All 49 subjects were selected for the training program. Four were unable satisfactorily to pass the American Optical Company

3 Lancaster, W. B. Present Status of Eye Exercises for Improvement of Visual Functions, *Tr Am Acad Ophth* 48:413-424 (July-Aug) 1944.

4 Pseudo-Isochromatic Plates for Testing Color Perception, Southbridge, Mass., American Optical Company, 1940. Gallagher, Gallagher and Sloane^{1b}.

color vision test after ten hours of training and are omitted from our data, except for mention in table 2

Prior to the beginning of instruction, each student's response to each of the American Optical Company Pseudo-Isochromatic Plates and to each of the Ishihara plates⁵ was recorded. He was also asked to sort each of a group of colored glass beads into its proper compartment, and the time required and the number of errors made were noted. As a further estimation of color vision the reading on a desaturation test was determined, this test is described in detail later. No subject had further experience with the desaturation test until his training period was completed. At the close of these tests each student was shown the errors he had made in sorting the beads and was urged to study them carefully, he then attempted to correct his mistakes. He was also given sample colored slips from paint advertisement folders and was asked to study these. At every point the subject was urged to exercise care in making decisions, to avoid snap judgments and to refuse to accept the idea that he was handicapped.

TABLE 2—Data on Four Subjects Not Included in Other Tables Because of Failure Satisfactorily to Pass the American Optical Company Test After Ten Hours of Training*

Subject	American Optical Company Plates Failed		Ishihara Plates Failed	Beads		Initial Desaturation Test Rating	Hours of Training
	Entire Series	"Key" Plates		Errors	Time		
A L †	34	8	14	5	5 min	12.5	10
D A †	33	8	14	13	2 min 5 sec	11	10
R P ‡	35	8	14	12	5 min	11.5	10
W A §	32	7	14	2	4 min 3 sec	11.5	10

* Data on 1 subject (M D) are included in our final results despite the fact that his training required more than ten hours.

† The subject made 9 errors on the total series and 2 errors in the key plates of the American Optical Company and 14 errors on the Ishihara plates after ten hours' training, and the rating on the second desaturation test was 12.0.

‡ The subject did not return for a retest after ten hours of training.

§ The subject made no errors on the American Optical Company plates after ten hours' training but was unable to do the test in less than three minutes and thirty seconds and made 6 errors on the Ishihara retest, the final rating on the desaturation test was 11.

or incapable of making color discriminations. When these exercises were mastered, work was begun with color charts, which had been removed from the American Optical Company book of plates, so that random order could be obtained. The subject was instructed first to look for the dots of greatest contrast which vaguely outlined the numbers and then to attempt to trace from dot to dot with a cotton-tipped applicator. Differences in shades were indicated and explained, and continual tracing and retracing of the numbers were practiced. Individual lessons were given two or three times a week. When the subject was apparently able to go through all the test plates accurately and quickly, he was given a formal test on all the 46 plates, and if all were read correctly within a two minute period, he was considered to have passed and put through a final trial on the Ishihara plates and the desaturation test.

A schematic diagram of the desaturation apparatus is shown in figure 1. Two voltage-regulated sources of incandescent illumination, A and B, are used. The

5 Ishihara, S. The Series of Plates Designed as Tests of Colour Blindness, ed 6, Chicago, C H Stoelting Company, 1932.

unfiltered light from *B* is focused by a lens and reflected from the semitransparent mirror, *I*, so that at the aperture, *K* ($\frac{1}{2}$ inch [1.27 cm] in diameter), it is somewhat larger than the aperture itself. Light from source *A* passes through filter *E* (Filter, Jena no RG1, 2 mm, approximating Signal Red) or filter *F* (Filter, Jena no BG7, 2 mm, approximating Signal Green), whichever it is desired to present. The light then passes through a neutral wedge, *G*, of variable density, compensated, the position of which determines the amount of colored light allowed to pass to the partially transmitting mirror, *I*. This beam of light is also focused

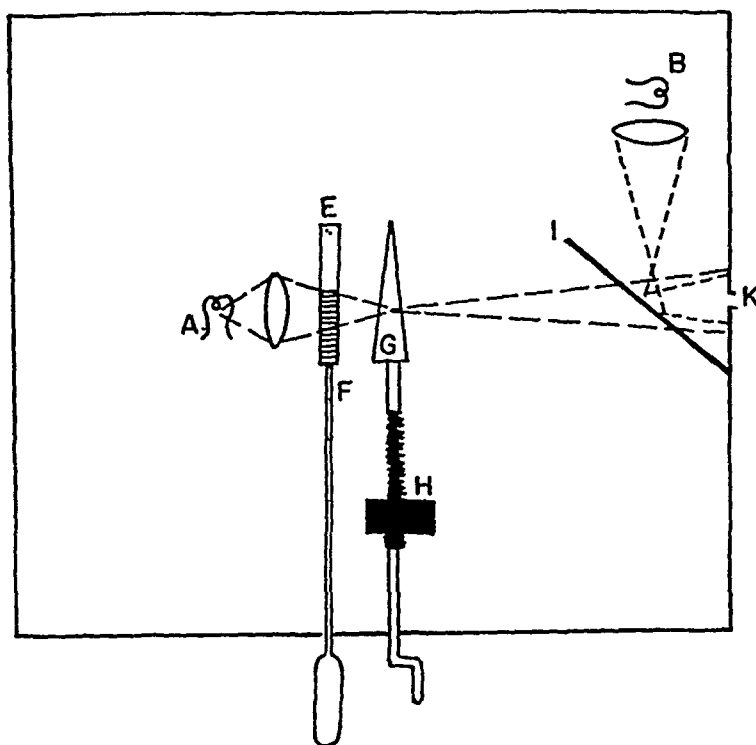


Fig 1—A schematic diagram of the desaturation apparatus

TABLE 3—Percentage of Colored Light Which Was Transmitted by the Wedge for Each Successive Desaturation Test Rating Value

Desaturation Test Rating	Percentage of Colored Light Transmitted
7	1.1
8	1.9
9	3.4
10	6.0
11	10.5
12	18.5
13	25.0
14	57.0

to a circle of the same size as that of the unfiltered light. A piece of "ground cellulose acetate," used as a diffusing screen, is placed over the aperture, *K*. The brightness and apparent angular size of the light are such that foveal vision is used. The neutral wedge, *G*, can be positioned, with considerable accuracy, by means of a screw mechanism, *H*, which permits varying amounts of colored light to be transmitted. At rating 8, for example, the wedge transmitted only about 2 per cent of the colored light, whereas at reading 11 about 10 per cent was transmitted (table 3).

As may be inferred from the diagram and the foregoing description, a white light of constant intensity appears at all times on the diffusing screen. By changing the position of the neutral wedge, different saturations of red and green may be obtained. The test is presented in a darkened room, the subject to be tested being seated 12 feet (3.6 meters) directly in front of the aperture screen. All movements of the operator are concealed from the view of the subject. A high saturation first of red and then of green is exposed in order to show the subject the sort of test with which he is dealing. It is explained to him that at very low saturation he will doubtless be unable accurately to identify the colors but that he must "guess" either red or green, regardless of this. A very low saturation is set up to start with, and red and green exposures are given in

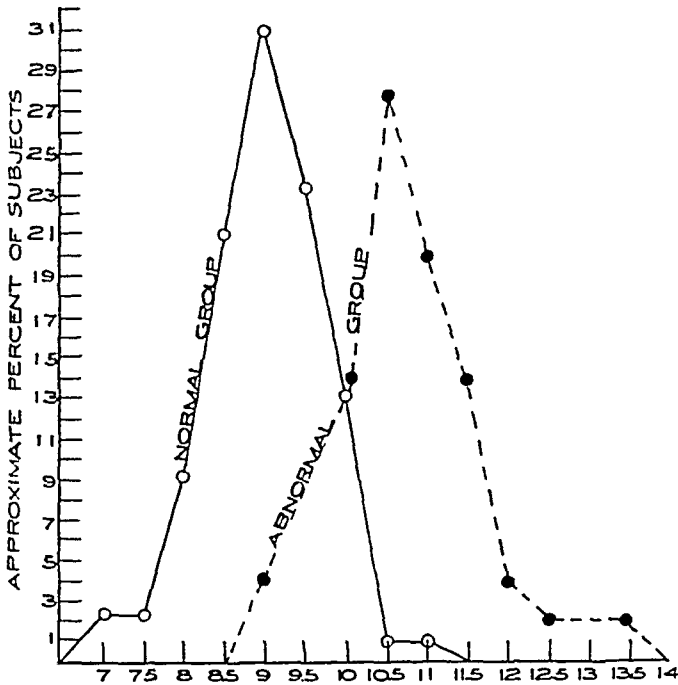


Fig 2—The curve of solid lines and circles shows the approximate per cent of the group with normal color vision (111) for each desaturation test rating, and the curve of broken lines and dots gives similar information for the group (49 subjects) whose color vision was abnormal

random order, previously determined by tossing a coin. As soon as the subject makes an error in identification, a new series of exposures is started at the next higher level of saturation. The position of the neutral wedge when the candidate is first able to identify the colors twenty consecutive times without a mistake is recorded as his rating on this test.

Results—The normal range of desaturation test ratings of 111 subjects who gave correct responses to the American Optical Company Pseudo-Isochromatic Plates, and who were therefore presumed to have normal color vision, were obtained. Their responses ranged from 7.5 to 11.0, the mean being 9.04 ± 0.04 . The reliability of the test ratings can be gaged by analysis of the data obtained on 129 subjects, including 45 persons with abnormal color vision who were tested

and retested. The coefficient of reliability was derived by the Pearson product moment method and is 0.763. The distribution of initial results on the desaturation test on 111 normal and 49 abnormal subjects is

TABLE 4—Data Concerning the Forty-Five Subjects Given Color Vision Training

Name *	American Optical Company Plates Failed		Ishihara Plates Failed		Beads Before Training		Desaturation Test			Number of Train- ing Hours Re- quired
	Entire Series (46)	"Key" Plates (10)	Before Train- ing	After Train- ing	Result	Time	Before Train ing	After Train ing	Change †	
R L	21	4	13	0	No errors	3'	9	8	+1	2
N P	24	5	11	2	No errors	1' 45"	9	9	0	2
B V	19	3	9	4	No errors	2' 50"	9½	9½	0	2
F P	10	3	8	2	No errors	2'	9½	8½	+1	2
J L	10	1	9	2	No errors	2'	9½	9	+½	2
O G	11	1	11	1	No errors	2'	9½	9½	0	3
R W	20	3	10	0	No errors	1'	9½	9½	0	2
W O	20	3	9	6	No errors	2'	10	9	+1	2
R B	18	6	9	2	No errors	1' 5"	10	10	0	2
F B	12	2	9	0	No errors	2'	10	10	0	1
A T	13	3	10	4	No errors	2' 5"	10	11½	-1½	1
H R	31	7	15	1	No errors	2' 45"	10	10	0	7
G D	35	8	15	15	14 errors	4' 30"	10	11	-1	13
A M	29	4	13	0	2 errors	6'	10	11	-1	10
L K	31	7	14	9	12 errors	2' 15"	10½	10½	0	9
S A	26	5	11	1	2 errors	1' 20"	10½	10½	0	3
J W	29	5	15	3	No errors	3'	10½	11	-½	5
A A	38	6	15	2	No errors	1' 18"	10½	11½	-1	5
W W	20	3	8	0	No errors	3'	10½	9½	+1	4
B H	25	4	15	7	2 errors	4' 15"	10½	10	+½	8
A C	35	7	15	7	1 error	4'	10½	11	-½	3
L B	31	5	13	2	No errors	1' 30"	10½	11½	-1	6
G McL	36	8	15	4	5 errors	4'	10½	11½	-1	5
E L	38	8	14	6	12 errors	1' 30"	10½	11½	-1	9
D H	32	6	14	9	14 errors	2'	10½	10½	0	9
R M	35	8	13	6	No errors	2'	10½	10	+½	4
R P	33	8	15	2	1 error	2'	11	11½	-½	6
B M	29	7	15	7	12 errors	4'	11	10½	+½	9
F G	8	2	11	5	No errors	1' 30"	11	11	0	2
H P	23	7	13	3	No errors	2'	11	11	0	1
G C	19	5	11	0	No errors	1' 30"	11	10½	+½	3
A L	30	6	15	5	No errors	2' 15"	11	11	0	4
W B	29	6	13	3	3 errors	5'	11	11	0	7
R McK	35	8	15	15	14 errors	3'	11	11	0	7
W A	37	7	15	5	5 errors	4' 25"	11½	11	+½	8
A McL	27	5	15	4	2 errors	2' 30"	11½	11	+½	2
C T	30	5	15	3	No errors	3'	11½	11½	0	4
A C	32	6	14	1	12 errors	3' 15"	10½	10	+½	10
C S	35	8	15	5	25 errors	6'	10½	12½	-2	8
L V	28	5	11	1	2 errors	3'	11	11½	-½	3
A H	32	7	15	6	2 errors	3' 45"	11½	10½	+1	7
C B	37	8	15	9	12 errors	4'	11½	10½	+1	8
B H	34	8	15	2	16 errors	3'	12	10½	+1½	6
R S	37	6	15	11	No errors	3'	12	11	+1	10
R P	35	7	14	10	25 errors	2'	13½	14	-½	8
Range	8-39	1-8	8-15	0-15	0-25	1' 6'	9-13 5	8-14 0	-2 +1 5	1-13
Mean and probable error	27.04 ±0.85	5.47 ±0.21	12.89 ±0.24	4.27 ±0.37	4.33 ±0.68	2.96' ±0.12'	10.59 ±0.08	10.58 ±0.11	+0.01 ±0.07	5.70 ±0.31

* The names are arranged in the order of their rating on the first desaturation test. At the end of the training period all these subjects gave the correct responses to the 46 American Optical Company plates within two minutes.

† An improvement in the desaturation test rating following training is indicated by the plus sign, a decline, by the minus sign.

shown in figure 2. That the American Optical Company test and the desaturation test discriminate in the same fashion between persons whose color vision is weak and those whose color vision is normal is shown

by the correlation 0.82 between the initial American Optical Company test rating and the initial desaturation test rating of the combined group, made up of 111 with normal and 49 subjects with weak color vision.

The number of hours of training required to bring each boy to the point where he could satisfactorily pass the American Optical Company color test is given in table 4, together with the number of key plates and the total number of plates failed before training, the number of Ishihara plates failed before and after training, the number of errors made and the time required for bead sorting before training. Boys quickly learned to complete the sorting of beads, consequently, a record of their performance on this test after training is omitted.

The fact that 45 out of the 49 boys who failed the color vision test were subsequently, after a series of not more than ten training sessions, able satisfactorily to pass this test is of considerable significance. The question at once arises whether these subjects' color perception had undergone a change because of the training methods employed or whether only their ability to interpret the test numbers had changed. It will be noted (table 4) that only 6 of the 45 boys made no errors on the second Ishihara test given at the end of the training period. Training on the American Optical Company plates had improved their ability to interpret the Ishihara plates, but errors were still made by the subjects on this very similar test. The mean number of Ishihara plates failed before training was 12.89 ± 0.24 , and, although the number of the American Optical Company plates failed after training had dropped to zero, the mean number of Ishihara plates failed fell only to 4.27 ± 0.37 . Before training the correlation between the number of American Optical Company plates failed and the number of Ishihara plates failed was 0.83 ± 0.03 and that between the key American Optical Company plates and the Ishihara plates 0.85 ± 0.03 , but after training these correlations were obviously lost.

No significant change in rating on the desaturation test followed the training period. Sixteen boys made some improvement, 16 had the same rating, and 13 had a lower rating, on the desaturation test after training. The mean rating on the desaturation test given subjects with abnormal color vision before training was 10.59 ± 0.08 , and the mean of the ratings after training was 10.58 ± 0.11 , a difference of only 0.01, whereas the difference between the first tests given to normal and to abnormal subjects was $+1.55 \pm 0.09$, giving a critical ratio of 17.22.

Fifteen boys given training which resulted in their ability to pass these tests in December 1943 were retested in May 1944 (table 5). None of these had been given further training in that interval, but 5 passed these tests as part of their examination for various specialized branches of the armed services. On our retest, only 5 made no errors

on the key plates, and only 2 read all 46 plates correctly. All made the same or a poorer response to the desaturation test, only 3 made no errors on the Ishihara test. The effect of training apparently does not persist. These results are comparable to the experience which the armed services have had with men who had been given color vision training. Some failed badly in critical situations which demanded accurate color perception.⁶

II TRAINING ON DESATURATION TEST

Training on the American Optical Company test plates developed the ability to pass that test but did not result in an increased ability to interpret the colors of the desaturation test. The question arose

TABLE 5—*Results on Retesting in May 1944 Fifteen Subjects Who Had Successfully Finished a Training Period in December 1943*

Subject	Desaturation Test Rating		American Optical Company Plates Failed		Ishihara Plates Failed	
	Directly After Training	Five Mo After Training	Five Mo After Training		Directly After Training	Five Mo After Training
			Entire Series	Key Plates		
W B	11	11	3	1	3	6
C B	10½	11½	10	1	9	9
A C	10	10½	8	2	1	9
G G	9½	9½	1	1	1	2
B H	10	10½	2	0	7	4
D H	10½	10½	2	0	9	6
J L	9	9½	0	0	2	0
R L	9	9	5	1	0	2
R McK	11	11	13	2	15	13
R M	10	10½	11	2	6	8
W O	9	10	0	0	6	8
R S	11	12	7	1	11	12
F P	8½	9½	2	1	2	1
W W	9½	10½	1	1	0	0
R W	9½	9½	1	0	0	0

whether a period of training on the desaturation test would improve the ability to interpret the American Optical Company test. This investigation seemed particularly desirable because the conditions of the desaturation test are roughly similar to those life situations (i.e., signal lights) in which the aviator, navigator or locomotive engineer has to discriminate correctly, although the varying conditions (while moving at great speed, in fog, etc.) in which these men have to make quick, accurate decisions were not simulated. One who attempts to improve the abnormal color vision of a trainee needs to keep in mind the type of color discriminations which he may subsequently have to make and the conditions under which he may have to make them.

Method—Six boys, ranging in age from 15 to 17 years, were chosen for training on the basis of their initial performances on the American Optical Company Pseudo-Isochromatic Plates and on the desaturation test. None of those

⁶ Berens, C., in discussion on Lancaster,³ p. 422

selected had failed less than 6 of the key American Optical Company plates, none had a rating of better than $11\frac{1}{2}$ on the desaturation test, and none had any previous training on either the color plates or the desaturation test

All training was done with the desaturation test device alone. Color plates were used only in the initial and the final testing procedures. At the initial training session the subject was first repeatedly shown the red (and then the green) light at a level of desaturation one step above his previously determined threshold. This was done to increase his confidence and thoroughly to familiarize him with the quality of the lights and the differences between them. When rapid, accurate responses were made at that level, the amount of colored light was decreased by

TABLE 6—Data on Six Boys Before and After Training on the Desaturation Test Device *

Name	No of Training Periods	Desaturation Test Rating	Steps in Desaturation Test Rating	No of Plates Failed		
				American Optical Company		Ishihara
				"Key" Plates	Total Series	
A S	10					
Before		13		6	21	11
After		$10\frac{1}{2}$	5	7	23	15
L L	7					
Before		$12\frac{1}{2}$		7	21	13
After		$9\frac{1}{2}$	6	7	19	13
M L	10					
Before		12		6	21	15
After		10	4	6	17	13
G G	11					
Before		12		8	25	15
After		$11\frac{1}{2}$	1	6	15	13
D P	9					
Before		12		6	16	13
After		$10\frac{1}{2}$	3	6	15	13
O Mc	11					
Before		$11\frac{1}{2}$		8	27	15
After		9	5	6	19	15
Average	9.6		3.8			
Before		12.1		6.8	21.8	13.6
After		10.2		6.3	18.0	13.6

* No training on either the American Optical Company test plates or the Ishihara test was given these subjects

one step and practice was resumed. He was shown the red light (and subsequently the green light) five successive times at that level and urged to pay strict attention to its appearance. The red light was then again shown five times at that level and the green light once, then the green light five times and the red light once. Those procedures were each repeated twice. Next, alternate red and green lights were shown for a total of ten exposures. If after that period of attempting to acquaint him with the two lights he claimed to be ready for a test, he was then given a series of twenty exposures in random order. In the event of incorrect responses, the previous training was repeated, if correct responses were made, the per cent of saturation of the colored light presented was decreased another step. Twenty minute training periods were given four times a week. To avoid the effect of accessory aids to interpretation, the operator was screened from the trainee, and such factors as motion and sound were controlled.

Results—In table 6 are given the number of training sessions for each boy, his rating on the desaturation test before and after training, the difference, if any, between these two ratings, the total number of American Optical Company plates, and the number of key plates and the number of Ishihara plates failed before and after training on the desaturation test device. It is evident that 5 of the 6 boys made a significant improvement in ability to interpret the red and the green signal light of the desaturation test. The ratings of all but the 1 boy were within the normal range on that test, and 1 (O M) achieved a rating equal to the normal mean. It is significant that only 1 boy, after this training, had a rating as good as the mean for normal persons and that the ratings of the others, although within the normal range, fell at the upper end of the normal distribution curve (fig 2). Further improvement might have been obtained had the training extended over a longer period, but the impression was gained that each subject had reached what seemed to be his maximum capacity. Training was stopped when successive training sessions yielded no improvement. However, despite the definite increase in ability to interpret the desaturation test made by 5 of these 6 boys, none made any significant improvement in performance on the key American Optical Company or the Ishihara plates. Two showed improvement in the total number of American Optical Company plates failed, but even normal persons vary considerably in their responses to many of the plates in that series.^{1b} After training on the desaturation test, none failed less than 6 of the key plates, only 2 failed any fewer than they had initially, and yet all but 1 had shown considerable improvement on the desaturation test. It seems clear that although this training method is capable of improving the ability to interpret a signal light of red or green as presented in the desaturation test device, it does not result in a significant increase in ability to interpret the plates of the Ishihara or the American Optical Company color test. It appears that improvement of color vision for all situations cannot be obtained by either of these training methods.

SUMMARY

Forty-nine subjects who had been selected as weak in color vision on the basis of responses to the American Optical Company Pseudo-Isochromatic test plates were subsequently given training on those test plates until all but 4 could satisfactorily pass that particular color vision test. However, although after training perfect responses were made on the American Optical Company test plates by 45 members of this group, only 6 made perfect responses to all the plates in the very similar Ishihara test, and the scores on a color desaturation test, which also had not been practiced, did not improve. A retest on the American Optical Company plates several months later showed a considerable

diminution in ability to make correct responses to these plates and indicated that the effects of this type of training may not long persist

Six other boys were given the desaturation test, the American Optical Company and the Ishihara color plate tests before and after a period of training on the desaturation device. Five of these subjects showed improvement in their ability to interpret the red and green lights presented by that device after a small number of training periods, but none showed a significant degree of improvement in interpreting the color vision test plates

Color vision training apparently is successful in enabling most persons with weak color vision to respond correctly to such a test as the American Optical Company plates or the desaturation test herein described, but from this study there is no evidence that either of the training methods used improved the capacity to discriminate between colors in other than the situation in which training was given. Training which enables a person (previously classified as deficient in color vision) to achieve a test rating comparable to that of persons who have normal color vision apparently does not result in the development of the ability to differentiate colors in all situations and under all conditions with the accuracy and speed possessed by those who have normal color vision

EXPERIMENTAL STUDIES ON THE BLOOD-AQUEOUS BARRIER

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II Electrophotometric Measurements of Fluorescein Content of Aqueous After Intravenous Injection of Fluorescein, the Eye Being Under the Influence of Physostigmine, Pilocarpine, Neostigmine or Atropine¹

IT HAS been demonstrated by numerous authors, especially by the splendid work of Duke-Elder² and Friedenwald³ and their co-workers, that the penetration of the various constituents of aqueous through the blood-aqueous barrier follows a rather complicated scheme. Electric charge, size of the molecule and possibly other factors influence the ratio of transmission of each constituent. But, on the other hand, it has also been shown that any change of the permeability of the blood-aqueous barrier will affect all constituents to a certain extent, though not equally, whether they are electrolytes, nonelectrolytes or proteins. To mention only two examples, Krause, Yudkin, Stevens, Burmell and Hughson⁴ found an increase in the amount of arsenic present in the aqueous after intravenous injection of arsphenamines if the eye had been previously pilocarpinized, and Adler⁵ demonstrated a decrease in the permeability of the blood-aqueous barrier to protein in spite of the irritation brought about by the application of ethyl morphine hydrochloride (Dionin) if the eye had been atropinized previously. So far as water is concerned,

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1 Stocker, F W. Experimental Studies on the Blood-Aqueous Barrier I. New Electrophotometric Method of Measuring the Concentration of Fluorescein in the Aqueous, *Arch Ophth* **36** 612 (Nov) 1946

2 Duke-Elder, S, and Davson, H. The Significance of the Distribution Ratios of Nonelectrolytes Between Plasma and the Intraocular Fluid, *Brit J Ophth* **27** 432, 1943. Duke-Elder, S, Quilliam, J C, and Davson, H. Some Observations on the Present Position of Our Knowledge of the Intraocular Fluid, *ibid* **24** 421, 1940

3 Friedenwald, J S. Dynamic Factors in the Formation and Reabsorption of Aqueous Humor, *Brit J Ophth* **28** 503, 1944. Friedenwald, J S, and Stiehler, R D. Circulation of the Aqueous. VII. A Mechanism of Secretion of the Intraocular Fluid, *Arch Ophth* **20** 761 (Nov) 1938

4 Krause, A C, Yudkin, A M, Stevens, M A, Burmell, W W, and Hughson, D T. The Influence of Drugs on the Transmission of Arsenic into the Aqueous Humor, *J Pharmacol & Exper Therap* **39** 153, 1930

5 Adler, F H. The Action of Atropine in Ocular Inflammations, *Arch Ophth* **55** 484 (Sept) 1926

the findings of Kinsey, Grant and Cogan⁶ seem to demonstrate that a dynamic state prevails in which water of the eye is constantly exchanged for water in the blood and vice versa, the classic conception of inflow of fluid from the ciliary body and iris and outflow through the canal of Schlemm representing only part of the mechanism of exchange. Probably an increase or a decrease in the permeability of the blood-aqueous barrier would also affect the exchange of water. Consequently, if one can demonstrate a change in the permeability using a tracer substance, such as fluorescein, this change may apply at least qualitatively, to all elements involved in the exchange between blood and aqueous. In the past the only disadvantage in using fluorescein has been the lack of a method of accurate measurement of the amount of fluorescein present in the aqueous. This disadvantage, I believe, has been overcome by introducing the electrophotometric method described in the first part of this study.

After the normal curve of transfusion had been established,¹ efforts were directed in the following experiments toward establishing curves showing the change in permeability of the blood-aqueous barrier through the action of the principal miotics and mydriatics by testing the concentration of fluorescein in the aqueous at various intervals after intravenous injection of sodium fluorescein.

EXPERIMENTS

As in the experiments with normal eyes (part I), albino rabbits were used, and 0.25 cc. of a 20 per cent solution of sodium fluorescein per kilogram of body weight was injected intravenously. One drop of one of the following solutions had been instilled previously three times a day for forty-eight hours, the last one being given two hours before the injection of fluorescein: 2 per cent pilocarpine nitrate, 0.5 per cent physostigmine salicylate, 5 per cent neostigmine methylsulfate, and 1 per cent atropine sulfate. At various times after the injection of fluorescein, 0.20 cc. of aqueous was aspirated with a small syringe and a fine, very sharp needle, the cornea having been anesthetized shortly before the puncture with 2 per cent cocaine.

For the benefit of investigators who wish to use this method, I should emphasize the necessity of evacuation of the aqueous with the least possible trauma. If the bulb is unduly compressed or a blood vessel torn, either at the limbus or in the iris, an excessive amount of fluorescein is found. Readings in such cases are then out of line and must be discarded.

The readings of fluorescein on the photofluorometer obtained with the various specimens of aqueous are recorded in chart 1. The curves represent average readings. It would have been confusing to record all individual readings on the chart, as it contains several curves. Although the readings of course differed somewhat, there was no read-

⁶ Kinsey, V. E., Grant, M., and Cogan, D. Water Movement and the Eye, *Arch. Ophth.* **27**: 242 (Feb.) 1942.

ing below the normal average except for one reading for neostigmine, which was 6 after three minutes

As previously reported,¹ the readings were most reliable within the ten minute period after injection of fluorescein, after which time they become irregularly increased. This observation, made with animals which were not under the influence of any drug (part I), was confirmed in the present series. Therefore, this "critical" period was exclusively considered. Further investigation will be directed to a study of whether or not any useful information may be obtained from these irregularly increased readings.

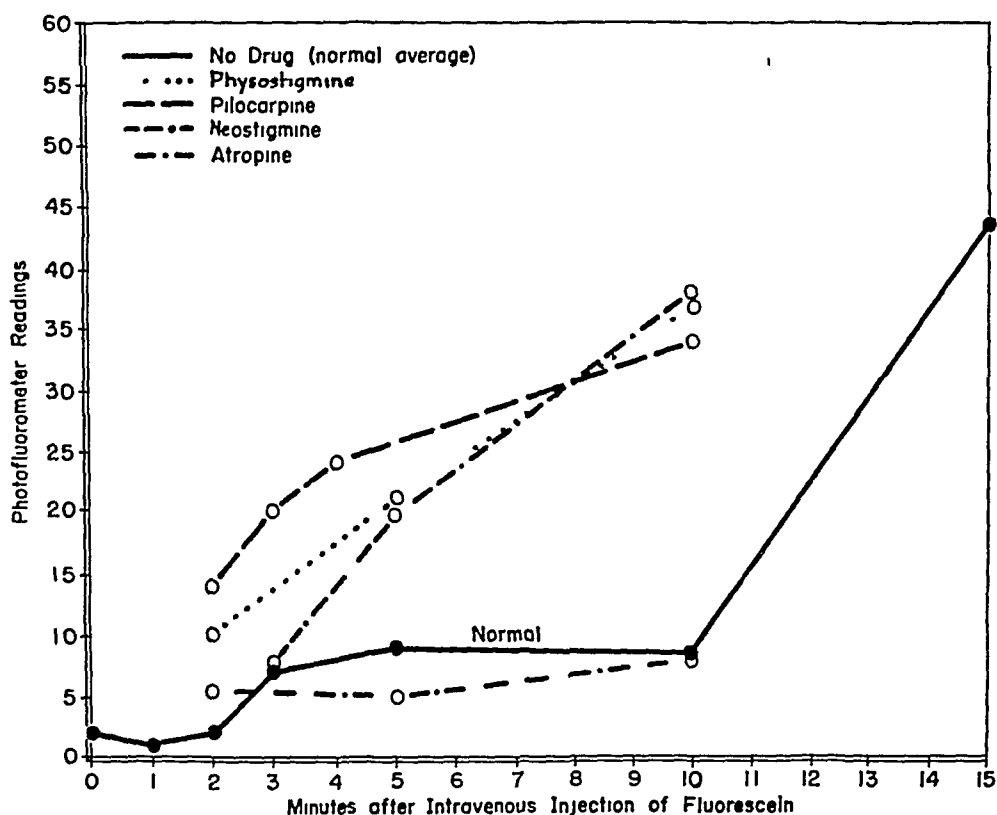


Chart 1—Influence of physostigmine, pilocarpine, neostigmine and atropine on transfusion of fluorescein into the anterior chamber

Two main facts are clearly evident. 1. All three drugs known as miotics, physostigmine, pilocarpine and neostigmine, increased the permeability of the blood-aqueous barrier for fluorescein when instilled into the conjunctival sac. 2. Atropine, on the contrary, did not increase the permeability of the blood-aqueous barrier, as all readings were slightly below the normal average.

Seidel⁷ already had found that after the instillation of physostigmine and pilocarpine there was an increase of proteins in the aqueous. This, of course, means that the permeability of the capillaries was increased.

⁷ Seidel, E. Ueber den Vorgang der physiologischen Kammerwasserabsonderung und seine pharmakologische Beeinflussung, *Arch f Ophth* **102** 366, 1920

Swan and Hart,⁸ who used inulin and fluorescein, found that physostigmine, carbaminoyl choline chloride and mecholyl (as well as epinephrine in the secondary phase) increased the permeability. However, they did not produce evidence with their method that pilocarpine would increase the permeability, although it increased the total solids in the aqueous. But the latter fact seems to show an increased permeability, at least for certain substances, which was confirmed by my photofluorometric readings.

Atropine in these experiments produced a slight decrease in total solids, an effect which also is consistent with my findings of decreased permeability to fluorescein. That Adler⁹ had found atropine to decrease the permeability of the blood vessels for proteins has previously been mentioned. It is generally believed that it is not a dilation or a constriction of the blood vessels which is responsible for the increase or decrease in permeability of the capillary walls, but a direct action of the drug on the endothelial cells (Seidel⁷).

The experiments with drugs whose influence on the permeability of the blood-aqueous barrier had already been proved demonstrated that the results with the new method on the whole concurred with previous reports and that the method was reasonably accurate if the necessary precautions in the technic were observed. I therefore thought it was safe to use it for the investigation of substances whose action on the blood-aqueous barrier had not previously been determined.

III Experiments Concerning Possible Influence of Rutin Given by Mouth on Permeability of Blood-Aqueous Barrier

Rutin ($C_{27}H_{30}O_{16} \cdot 3H_2O$) is a glucoside derived from flavonol. It was first isolated from tobacco at the Eastern Regional Research Laboratory, United States Department of Agriculture.⁹ It was found to be present, however, in a number of other plants and to be especially plentiful in buckwheat, as first discovered by E. Schmuck.¹⁰ Previously, Szent-Gyorgi and his co-workers¹¹ had extracted from lemon a substance belonging to the flavonol group for which they gave the formula $C_{28}H_{36-38}O_{17}$. They demonstrated that the administration of this substance would decrease the permeability of the capillaries for proteins.

8 Swan, K. C., and Hart, W. M. A Comparative Study of the Effects of Mecholyl, Doryl, Eserine, Pilocarpine, Atropine and Epinephrine on the Blood-Aqueous Barrier, *Am J Ophth* **23** 1311, 1940. ✓

9 Mr J. F. Couch, senior chemist, in charge of the tobacco section, made the complimentary release of the necessary amount of rutin for this experimental study.

10 Schmuck, E., cited by Couch, J. F., Naghski, J., and Krewson, C. F. Buckwheat as a Source of Rutin, *Science* **103** 197, 1946.

11 Armentano, L., Bentsath, A., Beres, T., Rusznyak, S., and Szent-Gyorgi, A. Ueber den Einfluss von Substanzen der Flavongruppe auf die Permeabilität der Kapillaren. *Vitamin P, Deutsche med Wchnschr* **62** 1325 1936.

as well as for water. It also prevented hemorrhages in certain cases of purpura. They called it citrin, or vitamin P (P stands for permeability). Because of the close chemical relationship of the two substances, citrin and rutin, the latter was tested clinically by Griffith, Couch and Lindauer¹² and by Griffith and Lindauer¹³ and was found to be similarly effective in conditions in which increased capillary fragility was present. In ophthalmology, rutin was reported to be effective in cases of hemorrhagic diabetic retinitis by Hanum¹⁴.

There is little doubt that the permeability of the blood-aqueous barrier plays an important part in certain cases of glaucoma. It also is known and confirmed by the experiments reported in part II of this study that the drugs generally spoken of as miotics not only contract the pupil but also increase the permeability of the blood-aqueous barrier. On the basis of the work of Kusel,¹⁵ Fortin¹⁶ and others, it is understood that the miotics reduce the tension by pulling the iris out of the chamber angle, thus widening the route of escape to the canal of Schlemm, and possibly by pulling on the scleral spur through the contraction of the ciliary muscle, with the same result. Whether the second type of action of the miotics, the increase of the permeability of the capillary walls, tends to increase or to decrease the tension is not so clearly evident. Clinical experience points to the possibility that either may happen. It is not intended to deal with these clinical facts in this experimental study, but the suggestion may be made that in certain cases the beneficial effect of miosis might be impaired or partially offset by the increased permeability of the blood-aqueous barrier. This explanation could clarify the cases in which miotics have no beneficial effect on the increased intraocular pressure, or have even an adverse one, as in the case mentioned by Luedde,¹⁷ in which physostigmine aggravated the condition. As rutin has been found to tighten the capillary walls, the possibility was to be considered that a combination of rutin and a miotic might improve

12 Griffith, J. Q., Couch, J. F., and Lindauer, M. A. Effect of Rutin on Increased Capillary Fragility in Man, *Proc Soc Exper Biol & Med* **55** 228, 1944.

13 Griffith, J. Q., and Lindauer, M. A. Effect of Chronic Lead Poisoning on Arterial Blood Pressure in Rats, *Am Heart J* **28** 758, 1944.

14 Hanum, S. Diabetic Retinitis. Clinical Studies of One Hundred and Ninety-Five Cases of Retinal Changes in Diabetics, *Acta ophth*, 1939, supp 16, p 3.

15 Kusel. Ueber die Wirkung des Ziliarmuskels auf das Ligamentum beim Glaucom, *Klin Monatsbl f Augenh* **44** 236, 1906.

16 Fortin, E. P. Schlemm'scher Canal und Ligamentum pectinatum, *Arch. de oftal de Buenos Aires* **4** 454, 1929, abstracted, *Zentralbl f d ges Ophth.* **22** 419, 1930.

17 Luedde, W. H. Relation of Capillary and Corneal Osmosis to Glaucoma Therapy, *Am J Ophth* **23** 388, 1940.

the pressure-reducing action of the latter in those cases in which the increase in permeability of the capillary walls would work to the contrary. Indeed, in a number of cases of glaucoma, I was able to reduce the tension considerably more when I gave the patient rutin by mouth together with a miotic in the eye than when I gave the miotic alone. A report on my clinical investigations carried out in connection with the glaucoma clinic of Duke University School of Medicine and the McPherson Hospital will be published shortly. In the present study I wanted to find out whether an influence on the permeability of the blood-aqueous barrier could be demonstrated in normal rabbits. Since rutin has a vitamin, rather than a pharmacologic, effect, a deficiency should be present in order to demonstrate its action, as most of the vitamins have no or little evident effect on the normal organism. But there was perhaps another possibility of demonstrating the tightening effect of rutin on the capillaries of the blood-aqueous barrier by creating first an increased permeability. In other words I could increase the permeability by instilling physostigmine, for instance, into the conjunctival sac of an animal which had been treated with rutin by mouth for some time, at the same time instilling the drug into the sac of another animal which had not received rutin. By testing the fluorescein of the aqueous with the photofluorometer after intravenous injection of fluorescein, I should be able to demonstrate whether there was a difference in the amount of fluorescein diffused through the blood-aqueous barrier in the 2 animals.

EXPERIMENTS

Four rabbits receiving the same diet were used. Two of them were given 10 mg of rutin by mouth twice a day for three weeks. This dose by far exceeds comparatively the usual dose for the adult man, which is 20 mg three times a day. As rutin is almost insoluble in water, there was no way of administering the accurate doses other than by feeding capsules. Dr William H. Anderson, intern in the ophthalmologic service, who undertook the feeding, invented an ingenious device by which the rabbits were made to swallow the capsules infallibly.

After three weeks of rutinization 0.25 cc of a 20 per cent solution of sodium fluorescein per kilogram of body weight was injected intravenously and the aqueous examined with photofluorometer within the ten minute period, as in the previous experiments. After that, the feeding of rutin to 2 of the rabbits was continued for two weeks longer. For the last two days 1 drop of 0.5 per cent physostigmine salicylate was instilled in each eye of the 4 animals three times a day, the last drop being given three hours before fluorescein was again injected in the same way and the aqueous tested with the photofluorometer. The readings are recorded in chart 2.

It may be noted that in the first part of the experiment the readings for fluorescein in the aqueous from the animals that had not received rutin (controls) concurred with the normal curve established previously (parts I and II). The readings for the animals that had been fed rutin were slightly below the readings for the controls at four and five minutes.

One earlier reading, at three minutes, was invalid, as an excessive amount of fluorescein was present, due to too much trauma from a blunt needle. This reading is so much out of line that it should be disregarded. I have recorded it only in order not to become guilty of suppressing any finding.

As to the second part, unfortunately, only 3 correctly collected specimens of aqueous could be obtained. One animal could not be used because an inflammatory reaction, combined with cataract in one eye,

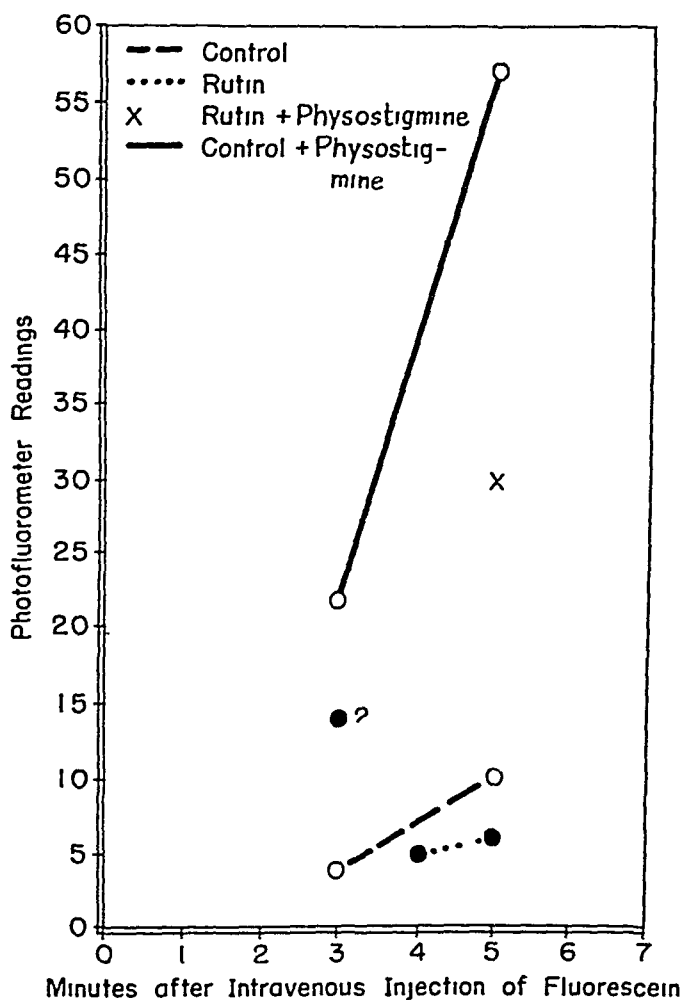


Chart 2—Influence of physostigmine and rutin alone and combined on trans-fusion of fluorescein into the anterior chamber

had set in after the first experiment. So only two readings for physostigmine without rutin and one reading for physostigmine with rutin could be recorded. However, the difference between the two readings at five minutes is so great, that for physostigmine alone being almost twice that for physostigmine with rutin, that attributing a certain significance to it seems justified.

In commenting on these results, I realize that a larger number of readings would be desirable, and I shall endeavor to follow up the

observations with more extensive experiments. As a preliminary report, the following conclusions seem to emerge.

1 No appreciable influence on the permeability of the blood-aqueous barrier can be demonstrated when normal rabbits are fed large doses of rutin for three weeks. If any influence is to be noted, it is in the direction of slight reduction in the permeability. However, the difference between the readings for the controls and those for the rutinized animals is too small to be significant. As mentioned previously, this negative result was expected. Rutin, having a vitamin rather than a pharmacologic effect, would need to meet a state of deficiency or alteration of the capillary walls in order for its influence to be demonstrated.

2 As far as the quantitatively limited present experiments would indicate, rutin given by mouth for several weeks seems to have a considerable tightening effect on the blood-aqueous barrier. The action of physostigmine, which is known to increase the permeability of this barrier after being instilled into the conjunctival sac, is greatly reduced if the animal has been rutinized previously.

Because of the small number of experiments involved, this report on the effect of rutin on the permeability of the blood-aqueous barrier is to be considered as only preliminary. However, in view of the far-reaching possibilities for the medical treatment of glaucoma, further experimental studies and clinical investigations appear to be justified.

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CORNEOSCLERAL SUTURE IN OPERATIONS FOR CATARACT

With Special Reference to the Incidence of Postoperative Hyphemia

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THE use of sutures for closure of incisions in cataract operations is one of the most useful and valuable refinements in ophthalmic surgery. First described by Williams¹ in 1860, it has become increasingly popular, until at present some type of suture is used in cataract operations in practically every large clinic in this country. Together with the routine use of akinesia and retrobulbar injections, the average ophthalmic surgeon has been able to obtain a greater percentage of successful results in cataract extractions than is otherwise possible.

A review of the literature on this subject shows that most authors are in agreement that sutures (1) promote prompt healing of the wound in most instances; (2) reduce the incidence of prolapse of the iris, (3) reduce postoperative glaucoma by permitting rapid reformation of the anterior chamber, (4) discourage epithelial ingrowth into the anterior chamber, (5) permit rapid closure of the wound, thus minimizing the loss of vitreous should that complication occur during operation, (6) decrease the amount of corneal astigmatism, (7) furnish greater security from postoperative complications in uncooperative patients, and (8) help to prevent cardiac failure and hypostatic pneumonia in aged and weak patients by allowing them greater freedom of movement after operation.

Ophthalmic surgeons do not all agree, however, that sutures aid in reducing the incidence of postoperative hemorrhage into the anterior chamber. Although this complication usually is not a serious one, it may, if severe, increase the number of days of hospitalization. It may also bring about toxic iridocyclitis, secondary glaucoma, staining of the cornea with blood or formation of a pupillary membrane, or it may infiltrate into the vitreous and remain there for an extended period, all of which complications can affect the final visual function or even result in loss of the eye. Older writers were of the opinion that the bleeding came from the iris.² More recent investigations,³ however,

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1 Williams, H W. Cataract Extractions, Arch Ophth 1 98, 1869

2 Wheeler, J M. A Study of Hemorrhage into the Anterior Chamber Subsequent to Operation for Hard Cataract, Tr Am Ophth Soc 14:742, 1916, cited by Philips^{3c}

(Footnotes continued on next page)

point to the incision as the source of hemorrhage. Most hemorrhages occur from the third to the sixth postoperative day. It has been shown⁴ that newly formed blood vessels are present in the incision as early as the second to the third day. Any separation of the lips of the wound tears these vessels, resulting in bleeding under the conjunctiva or, more frequently, into the anterior chamber. Many types of sutures have been devised to prevent separation of the wound, with its resulting complications. Among authors claiming success in reducing the incidence of postoperative hyphemia is Stallard,⁵ who, using a corneoscleral suture first described by Liégard,⁶ did not have a single case of hemorrhage into the anterior chamber in 107 consecutive cataract extractions. Prior to the use of this suture, 30 to 35 per cent of all his patients operated on for cataract in Moorfields had postoperative hyphemia. Philps,^{3c} using the same suture, was equally enthusiastic, reporting 120 consecutive cataract operations without hemorrhage. McLean,⁷ using a corneoscleroconjunctival suture modified and improved from a corneal suture described by Suarez de Mendoza,⁸ claimed an incidence of 3.6 per cent of postoperative hemorrhages into the anterior chamber in 110 cases, as against 10.7 per cent in 64 cases in which only conjunctival sutures were used. Others⁹ have reported comparable results in the reduction of postoperative hyphemia when using some type of corneoscleral sutures. On the other hand Ellett¹⁰ stated that he saw hemorrhages

3 Vail, D. (a) On Hyphema After Cataract Extraction, *Tr Am Ophth Soc* **31** 496, 1933, (b) On the Mechanism and Cause of Hyphema After Cataract Extraction, *Am J Ophth* **24** 920, 1941 (c) Philps, S. Post-Cataract Hyphema, *Brit J Ophth* **24** 122, 1940

4 Collins, E. T. Postoperative Complications of Cataract Extraction, *Tr Ophth Soc U Kingdom* **34** 18, 1914. Henderson, T. A Histological Study of the Normal Healing of Wounds After Cataract Extraction, *Ophth Rev* **26** 127, 1907

5 Stallard, H. B. A Corneo-Scleral Suture in Cataract Extraction. Its Technic and Advantages, *Brit J Ophth* **22** 269, 1938

6 Liégard, H. Une modification au procede de suture de la cornee dans l'operation de la cataracte, *Ann d'ocul* **149** 119, 1913, cited by McLean⁷

7 McLean, J. M. A New Corneo-Scleral Suture, *Arch Ophth* **23** 554 (March) 1940

8 Suarez de Mendoza, R. Nqueva\ faits de suture de la cornee dans l'extraction de la cataracte, *Bull et mem Soc franç d'opht* **10** 63, 1892, cited by McLean⁷

9 Leech, V. M., and Sugar, H. S. Reduction of Postoperative Complications in Cataract Operations with Corneoscleral Sutures, *Arch Ophth* **21** 966 (June) 1939. Kirby, D. B. Prevention and Handling of Complications Arising During and After Cataract Extractions. Some Practical Points, *ibid* **25** 866 (May) 1941. Lehrfeld, L., and Donnelly, E. J. Corneo-Episcleral Suture in Cataract Extraction, Correspondence, *ibid* **24** 401 (Aug) 1940

10 Ellett, E. C., in discussion on Peter, L. C. Sutures in Cataract Extraction, *Tr Am Ophth Soc* **45** 46, 1941

with unpleasant frequency in spite of the use of various types of sutures. Castroviejo, cited by DeVoe,¹¹ using three interrupted corneoscleral sutures, stated his belief that the incidence of hemorrhage in his cases had not decreased with its use. DeVoe,¹¹ in his statistical survey of 453 consecutive cataract operations, found postoperative hemorrhage into the anterior chamber in about 20 per cent of cases in spite of the use of various types of sutures. He also could detect no difference in the number of hemorrhages with conjunctival and with corneoscleral suture (types not described).

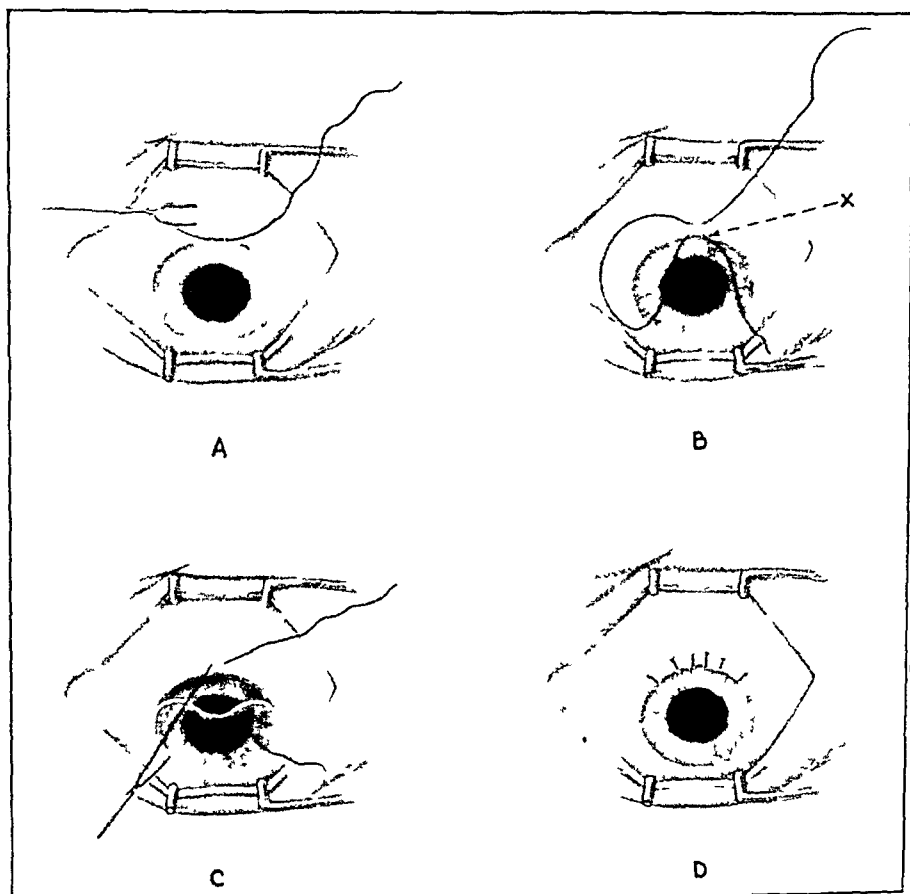
For the past fifteen years it has been the routine procedure in this clinic to employ three or more interrupted limbic-episcleral sutures for the closure of incisions in operations for cataract. The incidence of such complications as prolapse of the iris, delayed reformation of the anterior chamber and secondary glaucoma has certainly been reduced with their use. Hemorrhage into the anterior chamber, however, continued to occur with exasperating frequency. Past studies on the effect on the incidence of postoperative hyphemia of such factors as diabetes, arteriosclerosis, syphilis, hyperpiesis, blood coagulation and bleeding times and the vitamin C level of the blood did not yield any helpful information. DeVoe,¹¹ in a recent study, came to the same conclusions. In 1945 my associates and I began to use a modified Liégard suture placed at 12 o'clock on the limbus before the incision with the keratome was made, with two additional limbic-episcleral sutures placed on each side of it after extraction of the cataract. The reduction in postoperative hyphemia following the use of this stitch was significant enough to prompt a preliminary report on its use.

TECHNIC

After cocaineization of the eyeball, and before the retrobulbar injection of procaine, the 12 o'clock point on the limbus is marked with the tip of a toothpick dipped in gentian violet. This serves to indicate the point of introduction of the suture, as well as to preserve the landmark of the vertical meridian, since the globe tends to extort or intort after a retrobulbar injection. Fixation of the globe is accomplished by use of a Burch pick. The tip of the pick is placed opposite the point at which the needle is to penetrate the corneal tissue. With a 000000 black twisted surgical silk suture on a three-eighths circle taper or cutting point atraumatic $\frac{1}{2}$ inch (1.27 cm) needle, the bite is taken in the limbus at 12 o'clock just to one side of the gentian violet mark, the needle entering the corneal tissue sufficiently to insure a firm hold and coming out on the other side of the colored mark. The stitch is usually 1.5 to 2 mm wide. The thread is pulled through until stopped by a previously prepared double knot, about 3 cm from the end. The direction of the needle is then reversed, and, with fixation transferred to the

¹¹ DeVoe, G. Hemorrhage After Cataract Extraction, *Arch Ophth* 28: 1069 (Dec) 1942.

opposite side, a bite is taken about 1.5 to 2 mm above the first one, the needle passing through the conjunctiva and into the scleral tissue and out again. The scleral bite is equal in width to, and lies exactly opposite, the limbic stitch. This is really a mattress suture across the limbus at 12 o'clock. The suture is cut, leaving sufficient length for an adequate loop and a long enough end to permit easy grasp for quick closure of the wound when necessary. The ends and the loop of the suture are then dressed out of the line of incision to permit introduction of the keratome and scissors, without cutting the thread.



A, fixation with the Burch pick and introduction of an atraumatic needle into the limbus, *B*, modified Liegard suture in place (X knot near end of the suture), *C*, lifting of the corneal flap by pulling on the loop end of the suture to facilitate introduction of instruments into the anterior chamber, *D*, modified Liegard suture tied and interrupted limbic-episcleral sutures in place.

RESULTS

A review of the literature shows a wide variation in the incidence of postoperative hyphemia. DeVoe found that it ranged from 1 to 35 per cent, while Philips stated that the number of cases of hemorrhage into the anterior chamber was always higher in the series which were under the direct observation of the authors.

In the present series of 300 cases, dressings were changed twenty-four hours after the operation and daily thereafter. Particular attention was given to the presence of blood in the anterior chamber. Blood in the anterior chamber at the time of the first dressing was not considered the result of postoperative bleeding unless obviously of recent origin. Any sign of increased or new hemorrhage on subsequent dressing was recorded as postoperative hyphemia.

In the first 150 cases (table), three to five interrupted limbic-episcleral sutures were used. In 75 cases of this series a complete iridectomy was performed, whereas in the next 75 cases only a small peripheral iridotomy was done. No significant difference in the number of hemorrhages into the anterior chamber was found between these two series. In contradistinction to DeVoe's results, the type of operation on the iris apparently played no part in the incidence of hemorrhage into the anterior chamber.

Postoperative Hyphemia with Two Types of Sutures

Interrupted Limbic Episcleral Suture (150 Cases)					
	No. of Cases of Postoperative Hyphemia				
	Mild	Moderate	Severe	Total	Per Cent
Complete iridectomy (75 cases)	3	6	2	11	14.6
Peripheral iridotomy (75 cases)	3	5	4	12	16.0
Total	6	11	6	23	15.3

Modified Liégaard Suture (150 Cases)					
	No. of Cases of Postoperative Hyphemia				
	Mild	Moderate	Severe	Total	Per Cent
150 cases with peripheral iridotomy	6	3	1	10	6.6
Total	6	3	1	10	6.6

In the next series of 150 cases, the modified Liégaard stitch was used, in addition to the interrupted corneal-episcleral sutures. All cataracts were extracted through an intact sphincter pupillae, with a small peripheral iridotomy performed in each case. A comparison of the number of cases of postoperative hyphemia in the two series shows an incidence of 15.3 per cent in the first series and 6.6 per cent in the second, a decrease of over 50 per cent in the number of cases of hemorrhage into the anterior chamber in which the modified Liégaard suture was used. Moreover, in the first series the bleeding into the anterior chamber was mild in only one fourth of the cases and moderate to severe in the rest, whereas in the second series the hyphemia was slight in over

one-half the cases and moderate to severe in the others. Apparently, even if hemorrhage did take place when the modified Liegard stitch was used, it was more often a small one.

COMMENT

This report is concerned only with a comparison of the efficacy of the interrupted limbic-episcleral sutures and a modified Liegard suture in reducing hemorrhages in the anterior chamber. We have had no experience with the McLean suture,⁷ the Verhoeff tract suture¹² or other types of corneoscleral sutures, although these probably offer similar, and perhaps additional, advantages.

Perhaps the reason that use of the interrupted limbic-episcleral sutures is inferior in our hands is that not all of them are truly episcleral but are actually limbic-conjunctival. Those who have had experience with this type of suture know that it is not always possible to get a good bite of episcleral tissue with the needle. This is especially true in the aged. Moreover, an already sectioned globe makes the placing of sutures in the episcleral tissue a more difficult and hazardous procedure, so that occasionally the surgeon, rather than jeopardize the success of the operation, satisfies himself with a limbic-conjunctival suture. We have not infrequently seen sutures hanging loosely from the incision or dropping out altogether on the third to the sixth post-operative day. These probably were only limbic-conjunctival sutures, and not limbic-episcleral as intended. Thus, when strain is put on an incisional wound sutured with such stitches, the support which they should have given is absent. Separation of the lips of the wound, with tearing of the newly formed blood vessels, takes place, resulting in bleeding into the anterior chamber.

With the Liegard type of suture, a good limbic and scleral bite is assured. We have never seen this suture drop off spontaneously. One was inadvertently left in for three months and was still firmly in place when the eye was again seen. The interrupted limbic-episcleral sutures are of secondary importance, as the greatest stress on the limbic wound is in the region of 12 o'clock. Prolapse of the iris is more likely to occur between 11 and 1 o'clock than elsewhere. Frequently the stitch near each end of the incision is deliberately placed in the limbus and conjunctiva, as its main function is to furnish an air-tight wound so that a bubble of air may be injected and retained in the anterior chamber in cataract extractions with a round pupil. This procedure is used to keep the iris diaphragm in place and to prevent the formation of anterior peripheral synechias in the region of the incision.

¹² Verhoeff, F. H. Corneo-Scleral Suture in Operations for Cataract, *Tr Am Ophth Soc* 25 48, 1927.

Besides its effectiveness in reducing hemorrhages in the anterior chamber, we feel that the modified Liégard suture offers certain advantages¹³

- 1 The suture is simple and easy to place, no previous preparation, such as raising a conjunctival flap or making a groove in the limbus, with resultant annoying bleeding, being necessary
- 2 The assistant, by pulling on the suture loop on the corneal side opposite the knot, separates the lips of the incision, thus facilitating the introduction of instruments into the anterior chamber by the operator, such as scissors for enlarging the initial keratome incision, iris scissors for iridectomy or iridotomy and capsule forceps for grasping the lens
- 3 The wound may be closed quickly by simply pulling on the free end of the suture on the scleral side of the wound. This is of value especially when loss of vitreous is anticipated

Certain precautions must be kept in mind when this suture is used

- 1 The two horizontal bites must be placed as nearly opposite each other as possible to prevent lateral displacement of the two lips of the incision when the suture is tied
- 2 The stitch should not be tied too tightly or there may be buckling of the wound
- 3 If the keratome is used in making the initial incision in the limbus, the presence of an alert assistant is desirable in keeping the sutures near the scleral bite away from the edges of the blade. Otherwise the stitch may be cut accidentally

SUMMARY

A modified Liégard corneoscleral suture is described. Its use has reduced the incidence of hemorrhage into the anterior chamber in cataract extractions from 15.3 per cent, when interrupted limbic-episcleral sutures alone were used, to only 6.6 per cent, when this suture was added. In addition, when hemorrhages did occur, they were usually less extensive.

The other advantages of this suture are described, and precautions to be taken when using it are given.

¹³ We feel that the advantage of a prepared conjunctival flap in promoting better healing of the wound, as advocated by some authors, is dependent on the type of incision made, whether corneal or limbic. If it is corneal, the additional nourishment brought by a conjunctival flap to an avascular tissue certainly makes for better healing of the lips of the wound. On the other hand, a limbic incision, as practiced in this clinic, the initial incision being made with the keratome, which is entered about 1.5 mm. behind the limbus, and the section with scissors, usually with inclusion of a narrow tag of conjunctiva, make a prepared conjunctival flap unnecessary.

DANGER OF PENICILLIN THERAPY IN ACTIVE UVEITIS

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IN A SERIES of papers between 1929 and 1932, Fleming¹ observed that the growth of certain bacteria was inhibited by the chance introduction into the culture plates of the mold *Penicillium rubrum*, which is abundantly found in rotted fruit, vegetables and stale decaying matter. However, it was not until 1940 that great interest was stimulated in the field by the comprehensive, enthusiastic reports of Florey² and Abraham,³ together with their co-workers. Thereafter experimental and clinical studies appeared in the literature confirming the excellent results obtained with penicillin against certain bacterial infections.

STANDARDIZATION

For clinical application the mold had to be standardized, and two general methods of assay, or standardization, have been developed.

1 *Oxford, or Florey, Unit*—Florey and Florey⁴ employed *Staphylococcus aureus* plates incubated with *Penicillium* for twelve to sixteen hours at 37 C. The surrounding zone of bacterial inhibition was observed, and each 24 mm. zone was set up to be equivalent to 1 unit. This was later modified⁵ by using *Bacillus subtilis*, a more stable and sensitive organism than *Staph. aureus*, and one which gave larger and sharper borders of inhibition on the culture plates.

Read at a meeting of the New York Society for Clinical Ophthalmology.

1 Fleming, A. On Antibacterial Action of Cultures of *Penicillium*, with Special Reference to Their Use in Isolation of *B. Influenzae*, *Brit. J. Exper. Path.* **10** 226-236 (June) 1929. Fleming, A., and Maclean, I. H. On Occurrence of Influenza Bacilli in Mouths of Normal People, *ibid.* **11** 27-134 (April) 1930. Fleming, A. On Specific Antibacterial Properties of Penicillin and Potassium Tellurite, Incorporating Method of Demonstrating Some Bacterial Antagonisms, *J. Path. & Bact.* **35** 831-842, 1932.

2 Chain, E., Florey, H. W., Gardner, A. D., Heatley, N. G., Jennings, M. A., Orr-Ewing, J., and Sanders, A. G. Penicillin as Chemotherapeutic Agent, *Lancet* **2** 226-228 (Aug. 24) 1940.

3 Abraham, E. P., Chain, E., Fletcher, C. M., Gardner, A. D., Heatley, N. G., Jennings, M. A., and Florey, H. W. Further Observations on Penicillin, *Lancet* **2** 177-188 (Aug. 16) 1941.

4 Florey, M. E., and Florey, H. W. General and Local Administration of Penicillin, *Lancet* **1** 387-397 (March 27) 1943.

5 Foster, J. W., and Woodruff, H. B. Improvements in Cup Assay for Penicillin, *J. Biol. Chem.* **148** 723, 1943.

2 *Serial Dilutions*—In this method the concentration of penicillin required to inhibit the growth of *Staph aureus* in agar plates was determined⁶ One unit of penicillin per milligram just inhibited the growth of *Staph aureus* in dilutions of 1:50,000

An enzyme, penicillinase, inhibits the action of penicillin, although it probably does not destroy the drug⁷ This enzyme has been extracted from crushed *Bacillus coli* and other organisms Susceptible bacteria have been shown to develop a resistance to penicillin after repeated exposure McKee and Houck⁸ produced cultures of pneumococci type III which were resistant to thirty times the greatest amount of penicillin which previously just permitted growth The mechanism of this induced resistance was not clear, and no penicillin-destroying enzyme could be demonstrated⁹

Penicillin in vitro is about four times as potent as sulfathiazole against staphylococci and streptococci¹⁰ Although resembling the sulfonamide drugs in its action, penicillin possesses a number of advantages¹¹ 1 Its action is stronger 2 It is influenced relatively little by the number of bacteria to be inhibited 3 It is not hydrolyzed by pus 4 Its toxicity to tissue cells is low 5 Bacterial resistance is not developed as readily

Unfortunately, penicillin is destroyed by the hydrochloric acid of the stomach,¹² but if a duodenal tube is used to by-pass the stomach penicillin is absorbed by the intestine without damage to living cells¹³ Rectal administration is unsatisfactory because of the destructive action of penicillinase present in the bowel⁸ At room temperature penicillin solutions retain their potency for about one week¹⁴

6 Rammelkamp, C H Method for Determining Concentration of Penicillin in Body Fluids and Exudates, *Proc Soc Exper Biol & Med* **51** 95-97 (Oct) 1942

7 Abraham, E P, and Chan, E Enzyme from Bacteria Able to Destroy Penicillin, *Nature*, London **146** 837 (Dec 28) 1940

8 McKee, C M, and Houck, G L Induced Penicillin Resistance in a Pneumococcus Type III Culture, *Federation Proc* **2** 100 (March) 1943

9 Rammelkamp, C H, and Maxon, T Resistance of *Staphylococcus Aureus* to Action of Penicillin, *Proc Soc Exper Biol & Med* **51** 386-389 (Dec) 1942

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11 Herrell, W E Further Observations on Clinical Use of Penicillin, *Proc Staff Meet, Mayo Clin* **18** 65-76 (March 10) 1943

12 Rammelkamp, C H, and Helm, J D, Jr Excretion of Penicillin in Bile, *Proc Soc Exper Biol & Med* **54** 31-34 (Oct) 1943

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14 Kirby, W M M Stability of Penicillin Solutions at Room and Incubator Temperatures, *J A M A* **125** 628-629 (July 1) 1944

ABSORPTION AND ADMINISTRATION

Intravenous injection gives an immediate rise in the level of penicillin with a rapid fall, thus necessitating a continuous drip method in order to maintain a high level¹⁵ No penicillin reaches the cerebrospinal fluid, although some can be detected in the aqueous¹⁶ Intramuscular administration also causes a rapid rise in the blood level, with the peak remaining for thirty to forty-five minutes, followed by a gradual decline With this method the concentration in the aqueous is proportional to the dose, but a high level is never obtained, even with massive doses¹⁷ After paracentesis the level of penicillin in the secondary aqueous approaches that of the blood serum By this route injections should be given every three hours Subcutaneous absorption is very slow and somewhat painful A level of at least 0.156 Florey unit per cubic centimeter of serum is desirable for effectiveness against staphylococci, with lower levels required for streptococci Oral administration with the use of suitable capsules, such as cellulose acetate phthalate, to withstand the gastric secretions has been developed

Negligible amounts of penicillin reach the aqueous, vitreous and lens by any of the aforementioned methods of administration, and none is excreted in the tears¹⁸ Therefore other methods of administration have been employed in ophthalmology

Topical administration directly to the cornea and conjunctiva gives excellent concentrations on the anterior surface of the globe¹⁹ Preparations of 300 to 500 units per cubic centimeter in 0.9 per cent solution of sodium chloride are generally employed and should be given frequently, generally about every ten to sixty minutes, depending on the severity of the infection After constant corneal baths (20,000 units per cubic centimeter) in rabbits, high concentrations have been found in all portions of the eye except the vitreous, the posterior portion of the uvea and the retina²⁰ Von Sallmann^{18b} has been able to increase the concentrations of penicillin in the cornea, aqueous and iris with the use of iontophoresis,

15 Struble, G. C., and Bellows, J. G. Studies on the Distribution of Penicillin in the Eye, *J. A. M. A.* **125** 685-690 (July 8) 1944

16 von Sallmann, L., and Meyer, K. Penetration of Penicillin into the Eye, *Arch. Ophth.* **31** 1-7 (Jan) 1944

17 Town, A. E., and Hunt, M. E. Concentration of Penicillin in the Aqueous Humor Following Systemic Administration, *Am. J. Ophth.* **29** 171-175 (Feb) 1946

18 (a) Bellows, J. G. Penicillin Therapy in Ocular Infections, *Am. J. Ophth.* **27** 1206-1219 (Nov) 1944 (b) von Sallmann, L. Penetration of Penicillin into the Eye Further Studies, *Arch. Ophth.* **34** 195-201 (Sept) 1945

19 Scobee, R. G. Penicillin in the Treatment of Perforating Ocular Injuries and in Uveitis, *Am. J. Ophth.* **28** 380-387 (April) 1945

20 Herrell, W., and Heilman, D. Cytotoxic and Antibacterial Activity of Gramicidin and Penicillin Comparison with Other Germicides, *Am. J. M. Sc.* **206** 221-226 (Aug) 1943

but even with this method none could be detected in the vitreous or the lens

Cotton packs saturated with penicillin (500 units per cubic centimeter) and placed in the lower fornix^{18b} have proved satisfactory and provide a convenient method for obtaining high levels in the cornea, aqueous, iris and ciliary body. Depletion of penicillin in the ocular tissues usually occurs in about eight hours. Scobee¹⁹ suggested using 1.4 per cent instead of isotonic (0.9 per cent) solution of sodium chloride, since the former is isotonic with the tears. The addition of a wetting agent, such as zephiran chloride, has been found to increase the absorption.²⁰

Penicillin can be given subconjunctivally (500 units in 0.5 cc of isotonic solution of sodium chloride). This method is irritating but places the drug near the site desired. Rycroft²¹ advocated using larger doses (4,000 units) to speed diffusion and avoid producing resistance to penicillin. He reported 10 cases in which the aqueous was aspirated fifteen to ninety minutes after the subconjunctival injection and found that bacteriostasis of susceptible organisms in the aqueous was produced within thirty minutes. Penicillin can also be injected directly into the anterior chamber (200 units in 0.25 cc of solution of sodium chloride).

Local sensitivity to the drug after topical application was seldom experienced and then usually was not severe. Redness, thickening, ptosis and fissures of the lids have been described.²² Few systemic reactions of a severe nature have been encountered.²³ These untoward reactions have been urticaria, fever, transient azotemia, thrombophlebitis, chills, faintness and muscular cramps, but most of these reactions were thought to be due to the impurities in the preparation rather than to the penicillin itself.

PENICILLIN THERAPY OF OCULAR INFECTIONS

The value of penicillin for ocular infections has not yet been as clearly demonstrated as its usefulness in treatment of many systemic diseases, such as septicemia, meningitis and gonorrhea. At present the place of penicillin in ophthalmic therapeutics appears to be that of aiding, and possibly replacing, the sulfonamide compounds, which are limited in their use. It may be said that the sulfonamide drugs in ophthalmology have not lived up to the high expectations of a few years ago.²⁴

21 Rycroft, B. W. Subconjunctival Penicillin and Intra-Ocular Infection, *Brit J Ophth* **29** 501-511 (Oct) 1945

22 Vorisek, E. A., and Evans, A. L. Penicillin Administered Locally in Gonorrheal Ophthalmia. Sensitization Reaction, *Am J Ophth* **28** 520 (May) 1945

23 Lyons, C. Penicillin Therapy of Surgical Infections in the U. S. Army Report, *J. A. M. A.* **123** 1007-1018 (Dec 18) 1943

24 Chance, B. A Clinician's Experience with Sulfanilamide, *Am J Ophth* **23** 900-904 (Aug) 1940. Heath, P. Chemotherapy in Ophthalmology, *J. A. M. A.* **124** 152-155 (Jan 15) 1944

Only for those ocular infections in which cultures of penicillin-susceptible organisms have been obtained has the drug shown itself to be of proved value, and this is all that one should expect. Thus, in cases of ophthalmia neonatorum excellent results have been reported with the use of penicillin locally. Sorsby²⁵ studied a series of 85 cases, and in all instances in which full treatment was given he obtained rapid cures. He advocated local instillation of penicillin (2,500 units per cubic centimeter) every five minutes until the tendency for pus formation was controlled, after which the medication was given hourly.

Penicillin also has been found to be a therapeutic aid in cases of trachoma, again an infection of the external eye. Darius²⁶ treated both the acute and the chronic form with penicillin topically in a 1:500 dilution and had uniformly good results. In all these conditions good results had also been reported with sulfonamide therapy.

Except in some of the infections of the external eye, cultures of penicillin-sensitive bacteria are rarely obtained. Isolation of an organism is difficult in the case of inflammatory diseases of the cornea, uvea, lens, vitreous, retina, choroid and sclera, which today constitute the more serious ocular conditions encountered. Reports by various authors on the value of penicillin in treating the infectious conditions of the inner eye have not been in agreement.

Excellent results were obtained by Mietus²⁷ in 3 cases of severe ocular trauma with developing ciliary injection. In each case typhoid vaccine was given intravenously and atropine locally in addition to the penicillin, and in each instance the eye quieted rapidly. In conclusion, he expressed the opinion that "penicillin is a wonderful new therapeutic agent." Cashell²⁸ also reported a cure in a case of an infected injured eye following the use of penicillin both topically and by injection into the anterior chamber. Subsidence of the inflammatory process in an eye with endophthalmitis and hypopyon of spontaneous origin²⁹ has also been described, although the final vision was poor. The patient was also given sulfadiazine intravenously, sulfamerazine orally and atropine locally. The authors concluded that the penicillin was of value, but it would appear difficult to judge whether the sulfonamide therapy

25 Sorsby, A. Penicillin in Ophthalmology. Interim Review, *Brit J Ophth* **29** 511-536 (Oct) 1945.

26 Darius, D. J. Penicillin Treatment of Trachoma. Preliminary Report, *Am J Ophth* **28** 1007-1009, 1945.

27 Mietus, C. A. Ocular Therapy with Penicillin Used Topically, Intracocularly, and Systemically, with Case Reports, *Am J Ophth* **28** 173-179 (Feb) 1945.

28 Cashell, G. Treatment of Ocular Infections with Penicillin, *Brit M J* **1** 420-421 (March 25) 1944.

29 Green, M. I., and Jakobovits, R. Enophthalmitis Subsiding After Treatment with Penicillin, *Am J Ophth* **28** 191-193 (Feb) 1945.

or the penicillin, or perhaps neither, was the important therapeutic factor

Uveitis—The most frequent inflammatory process of the inner eye is uveitis. Reports on the treatment of this condition with penicillin have come chiefly from the military services, since penicillin was available earlier in military than in civilian practice. Scobee¹⁰ found that the administration of 150,000 units of penicillin intramuscularly for five to twelve days had a pronounced effect in 75 per cent of his series of cases of nongonococcic uveitis. The number of cases could not be given, for reasons of military security. In his discussion, he stated, however, that "if the patient received nothing but systemic penicillin plus atropine drops, relapses would invariably occur in five to seven days" and that "in no instance was a complete cure effected with penicillin alone." It appears that other therapeutic measures were employed in conjunction with penicillin and that the author questioned whether penicillin would be of benefit if used alone.

A combined comprehensive report from five hospitals of the Army Air Force on the treatment of nonspecific uveitis with penicillin was reviewed and analyzed by Irvine and associates³⁰. Fifty-six cases were collected, in all of which the condition was treated similarly with intramuscular injections of penicillin. Only in cases of acute iridocyclitis (16 cases) was significant improvement noted, but even in this group the author felt that "this improvement appeared to be no greater than would be expected with ordinary forms of treatment such as atropine, heat and foreign protein." The remaining 40 cases consisted of 15 cases of chronic iridocyclitis and 25 cases of acute and chronic choroiditis, and in only 2 of these (5 per cent) was there any significant improvement. It was concluded that penicillin was of questionable value in the treatment of uveitis.

At Fort Snelling, Minn., the most frequent cause of hospitalization in the ophthalmologic service was active uveitis. In service, patients with this condition were usually hospitalized, thus allowing the study and treatment of the patient to be as complete as desired. The treatment usually consisted in penicillin intramuscularly, atropine and hot packs locally and typhoid vaccine intravenously. In the 10 cases followed, the results were similar to those found by Irvine and associates,³⁰ who expressed their belief that penicillin did not influence the course of the disease and that improvement was no greater than with the usual therapeutic procedures.

However, 2 cases of unusual interest raised the question whether the penicillin therapy may actually have been detrimental to the uveitis.

³⁰ Irvine, S. R., and others. The Treatment of Non-Specific Uveitis with Penicillin, *Am J Ophth* 28 852-855 (Aug) 1945

REPORT OF CASES

CASE 1—A white man aged 43, single, while awaiting separation from the service, was referred to the hospital because of active iridocyclitis of the right eye of three days' duration. At the age of 21 he had acute urethritis, which was diagnosed as gonorrhea. Since then he has had frequent mild recurrences of the urethral discharge. During the past twenty years he had had at least ten attacks of iritis, occurring in one or the other eye. The patient was certain none of the attacks occurred before the onset of the original urethritis. Except for "arthritis of his back" for the past five years, for which he had never sought medical care, the history was otherwise without significance. He had never received penicillin.

Examination revealed moderate ciliary injection of the right eye, with vision of 20/70. Both new and old keratic precipitates were abundant, and posterior synechias were present. Details of the fundus could not be made out. The left eye was normal except for several old, well formed posterior synechias. Vision was 20/30. Tension was normal in each eye. He was placed under treatment with hot packs and atropine locally.

In the genitourinary service a thick, mucoid urethral discharge was found, which did not reveal organisms on smear or culture. It was believed that this was an old gonorrheal infection with residual chronic prostatitis. On the third day intramuscular injections of penicillin (150,000 units per day) were begun for this condition. All other studies revealed nothing abnormal except for mild hypertrophic arthritis of the lumbar vertebra. Intravenous typhoid therapy (25,000,000 to 45,000,000 organisms) was given every third day, with good systemic reactions. Scopolamine was substituted for atropine on the fifth day because of incomplete dilatation of the pupil. During the first four days improvement was noted, but then the eye became slowly and steadily worse, with reduction of vision to 20/400 and severe congestion and redness of the ciliary region.

The urethral discharge gradually subsided, and penicillin therapy was discontinued on the twelfth day. At this time the cornea was steamy, the iris muddy and the patient miserable. Tension had remained normal throughout. On the fourteenth day, two days after administration of penicillin had been stopped, the first improvement was noted, and during the next seventy-two hours the inflammation rapidly subsided. By the twentieth day, the eye was white, vision was 20/20—3, and details of the fundus were clear. No choroiditis was found.

CASE 2—A white man aged 25, single, was injured in the right eye by a fragment of glass from a broken bottle. Examination one hour later showed two lacerations of the cornea with involvement of 6 mm of the temporal sclera. A small bead of vitreous was presenting, and vision was limited to light projection. The bead of vitreous was excised, corneal and scleral sutures were placed, and a large conjunctival flap covering was made. Atropine and metaphen ointment were instilled locally.

On the second day intramuscular administration of penicillin was begun (150,000 units per day) as a prophylactic measure. Three days later a mild ciliary injection was noted, and this gradually increased. The conjunctival flap slowly withdrew, and the corneal and scleral sutures were found to be in good position. These were removed on the sixth day. The patient was given intravenous injections of typhoid vaccine every three days, together with atropine and hot applications locally, but the low grade uveitis persisted. The only positive history was an attack of gonorrhea two years before, which cleared rapidly with sulfonamide therapy and had not recurred.

By the sixteenth day the eye was neither better nor worse, vision was limited to counting fingers at 3 feet (120 cm), and at this time penicillin therapy was discontinued. Within forty-eight hours the patient felt more comfortable and the ciliary injection had begun to subside. On the twentieth day the eye could be readily opened and the uveitis had almost completely disappeared. Vision was 20/70, and fundus details were beginning to be discernible. Three days later he was transferred to another hospital for convalescent care.

COMMENT

Two patients with acute iridocyclitis were treated by the usual methods, with the addition of penicillin intramuscularly. In both the uveitis became progressively worse, and then on cessation of penicillin therapy, while use of typhoid vaccine and atropine was continued, the inflammatory process subsided rapidly. This may well have been coincidental. However, it is also very possible that the mechanism of the action of penicillin and the causative factors of uveitis have an intimate relationship.

PATHOGENESIS OF UVEITIS

The explanation that uveitis was simply the result of bacterial lodgings in the uvea from a focus of infection has not been satisfactory. The great weaknesses in this theory have been (1) little or no evidence of bacteremia in cases of uveitis, (2) a sterile aqueous and (3) no resemblance of the ocular lesions to those produced by staphylococci and streptococci.

As early as 1913 de Schweinitz³¹ expressed the belief that bacterial toxins played an important role in the causation of uveitis. Fuchs³² stated that the poisons, which must have access to the uveal tissue through the blood stream, were not likely to consist of micro-organisms, but more probably were their toxins, and most recent writers on the subject have agreed with this.³³

Experimentally, ocular sensitivity has been produced in rabbits by using bacterial products from dead streptococci,³⁴ an organism frequently suspected in the pathogenesis of this condition. Then, on injection of

31 de Schweinitz, G. E. Pathogenesis of Chronic Uveitis, Excluding the Syphilitic, Tubercular and Sympathetic Varieties, *Tr. Internat. Cong. Med.*, London (Sect. Ophth.) **17**, 1913, *Brit. M. J.* **2** 398 (Aug. 16) 1913.

32 Fuchs, E. The Pathogenesis of Chronic Uveitis, Excluding the Syphilitic, Tuberculous, and Sympathetic Varieties, *Tr. Internat. Cong. Med.*, London (Sect. Ophth.) **17**, 1913.

33 Jackson, E. Review of Literature of Chronic Uveitis, *Am. J. Ophth.* **14**: 1203-1209 (Dec.) 1931.

34 Rosenow, E. C., and Nickel, A. C. Results in Various Diseases from Elimination of Foci of Infection and Use of Vaccines Prepared from Streptococci Having Elective Localizing Power, *J. Lab. & Clin. Med.* **14** 504-512 (March) 1929. Brown, A. L. Chronic Uveitis. Bacteriologic and Immunologic Considerations, *Arch. Ophth.* **12** 730-750 (Nov.) 1934.

these same bacterial products at a remote site a typical uveal inflammation has resulted³⁵ Woods³⁶ injected bacterial vaccines prepared from organisms isolated from the focus of infection, with resulting exacerbation of the ocular inflammation. He suggested that the diseased eye may be hypersensitive to the bacterial products emanating from the primary focus of infection and that this might be the actual explanation of the uveitis³⁷

Irons³⁸ has shown that the phenomenon of sensitization was involved in recurrent uveitis. He expressed the belief that the exacerbation may well be due to bacterial toxins generated in the focus, which excite a reaction in the uveal tract, already specifically sensitized by the first attack.

ACTION OF PENICILLIN

It is generally agreed that penicillin is not only bacteriostatic but bactericidal³⁹. In studies on the staphylococcus with penicillin, actual lysis of the organisms has been demonstrated⁴⁰. Gardner⁴¹ described certain morphologic changes, such as spherical enlargement and elongation of the cells with increased length of chains, in gram-negative organisms after contact with penicillin.

Therefore in a case of active uveitis it can be presumed that products from dead bacteria are diffusing through the blood stream from a focus of infection, which frequently cannot be determined. These bacterial products or toxins, in turn, are causing an inflammatory reaction in the uveal tissue, which has become sensitized to these toxins.

On administration of penicillin systemically, it is known that some lysis occurs in those bacteria susceptible to penicillin, such as staphylococci, streptococci and gonococci, which also are the frequent etiologic agents in uveitis, according to present beliefs. The consequence of use

35 Zentmayer, W. The Prostate as a Remote Focus of Infection in Ocular Inflammations, *Tr Sect Ophth, A M A*, 1926, p 216

36 Woods, A. C. Allergy and Immunity in Ophthalmology, in Ridley, F., and Sorsby, A. *Modern Trends in Ophthalmology*, London, Butterworth & Company, 1940

37 Woods, A. C. Allergy and Immunity in Ophthalmology, Monograph 1, Baltimore, John Hopkins Press, 1933

38 Irons, E. E. Etiology of Chronic Iritis, *Am J Ophth* **14** 1228-1236 (Dec) 1931

39 Abraham, E. P., and Chain, E. Purification and Some Physical and Chemical Properties of Penicillin, *J Exper Path* **23** 103-115 (June) 1942
Herrell¹¹ Abraham and others⁸ Dawson, M. H., Hobby, C. L., Meyer, K., and Chaffee, E. Penicillin as a Chemotherapeutic Agent, *Ann Int Med* **19** 707-717 (Nov) 1943

40 Hobby, G. L., Meyer, K., and Chaffee, E. Observations on Mechanism of Action in Penicillin, *Proc Soc Exper Biol & Med* **50** 281-285 (June) 1942

41 Gardner, A. D. Morphological Effects of Penicillin on Bacteria, *Nature*, London **146** 837-838 (Dec 28) 1940

of penicillin is the release of more bacterial end products into the blood stream. Thus, in a case of active uveitis the use of penicillin may increase the amount of bacterial toxins in the blood stream by the destruction of bacteria in the focus of infection. This only adds new fuel to an already smoldering fire. If penicillin is discontinued, the production of new bacterial end products is stopped or greatly reduced, thereby breaking the vicious cycle inciting the uveitis.

Most cases of uveitis can be brought under control within a few weeks with the use of atropine, hot applications and some form of foreign protein therapy. Since most observers feel that penicillin is not of value in uveitis, it would seem more advisable not to employ the drug, especially when its use may actually be dangerous. It may be true that the foci of infection (they may be multiple) will be controlled or eradicated by the penicillin. If one believes that penicillin might be of value in clearing the suspected foci of infection, then the medication could be employed systemically a few months after the uveitis had subsided. In the meantime the patient should be under observation for an ocular recurrence.

In this report I have only tried to suggest an explanation for the exacerbation in 2 cases of uveitis treated with penicillin. The explanation has attempted to correlate present knowledge of the cause of uveitis with the action of penicillin on bacteria. Further studies certainly are needed on this subject.

CONCLUSIONS

- 1 Penicillin does not appear to offer any advantages in the treatment of uveitis as compared with previous methods.

- 2 Penicillin may cause the uveitis to persist longer than would otherwise be expected. Therefore the drug should not be used during the active inflammatory stage.

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RELATIVE DEFICIENCY OF PARASYMPATHOMIMETIC ACTIVITY IN AQUEOUS OF EYES WITH CHRONIC SIMPLE GLAUCOMA

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THE STUDIES of Loewi, Dale, Cannon and others have firmly established the validity of the concept of the chemical mediation of nerve impulses. It is now generally accepted that the effects of the somatic and parasympathetic nervous systems are produced by the liberation at the nerve endings of acetylcholine. This substance is quickly destroyed by cholinesterase, an enzyme present in the blood and tissue fluids. The effects of postganglionic sympathetic nerve impulses are the result of the liberation at the nerve terminals of epinephrine. The clinical implications of these findings are emphasized by the fact that in at least one disease, namely, myasthenia gravis, the primary dysfunction may be attributed to interference with the mechanism of acetylcholine activity.

The possible relation of these studies to the problem of glaucoma was suggested by several facts. Since the time of Laqueur, who in 1876 demonstrated the therapeutic effect of physostigmine on the elevated pressure of glaucomatous eyes, the administration of miotics has been the mainstay of the medical treatment of primary glaucoma. Pharmacologically, the miotics are parasympathomimetic drugs, and since their actions are similar to those produced by the release of acetylcholine at autonomic nerve endings they are sometimes referred to as cholinergic. They produce their effects either by a direct acetylcholine-like action on the effector cell or by inhibition of cholinesterase, with consequent prolongation of the effect of whatever acetylcholine may be physiologically present.

The classic theory that the hypotensive effect of these drugs on eyes with chronic simple glaucoma is attributable solely to the miosis they produce has been rendered extremely doubtful by more recent observations¹. That they play a more basic role in the restoration of the normal regulation of ocular tension has been suggested by recent experi-

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1 Duke-Elder, W. S. Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, p. 3392

mental studies of Bloomfield and Lambert² These investigations showed that pilocarpine, the most commonly employed of these miotic drugs, exerted a stabilizing effect on the abnormally increased lability of intraocular pressure which was demonstrated to be present in eyes with chronic simple glaucoma This regulatory effect occurred in a glaucomatous eye with a fixed pupil In nonglaucomatous eyes the physiologic stability of the ocular tension was not apparently influenced by this drug

Such observations suggested the hypothesis that some parasympathomimetic substance, such as acetylcholine, might be physiologically present in the normal eye and play a role in the mechanism of regulation of ocular tension As a corollary, it seemed possible that the abnormal intraocular pressure associated with chronic simple glaucoma might be associated with a deficiency in the activity of such a cholinergic substance The therapeutic effect of the miotic drugs in chronic simple glaucoma might thus be attributable to their ability to relieve to some degree such a diminution in parasympathomimetic activity in the eye Schoenberg³ previously had suggested on theoretic grounds that the administration of miotics in glaucoma might be a form of replacement therapy, similar to the use of insulin in diabetes mellitus

The purpose of this investigation was to determine experimentally whether a parasympathomimetic substance actually occurred in the nonglaucomatous human eye and to determine its identity if present. A series of eyes with chronic simple glaucoma was also studied to explore the possibility that some deficiency in the normal activity of such a cholinergic substance occurred in that disease. Since the aqueous humor is, in a sense, a perfusion fluid of the eye, and, with proper precautions, is safely obtainable by paracentesis from the living organ, the study of that fluid seemed suited to this purpose Because of the pharmacologic nature of this investigation and the extreme dilution of the substances which were studied, biologic methods of assay were employed

In 1930, Velhagen⁴ demonstrated that the aqueous humor of certain animals produced a sympathomimetic effect on the isolated frog heart Engelhart,⁵ one year later, instilled physostigmine into the eyes of rabbits to prevent the destruction by cholinesterase of any acetylcholine present and then exposed the eyes to light for parasympathetic stimulation Under these conditions, he proved by bioassay that acetylcholine was present in the aqueous humor of these animals In 1938, Pletneva,

² Bloomfield, S., and Lambert, R. K. Lability of Ocular Tension, *Arch Ophth* **34** 83 (Aug) 1945

³ Schoenberg, M. J. *Am J Ophth* **26** 1282, 1943

⁴ Velhagen, K. *Arch f Augenh* **103** 424, 1930

⁵ Engelhart, E. *Arch f d ges Physiol* **227** 220, 1931

Raeva and Voronina⁶ studied the biologic effect of the aqueous humor of human eyes and found that sympathomimetic activity was present in some and parasympathomimetic activity in others. They could demonstrate no consistent reaction of the aqueous in normal eyes or in any of the eyes with various pathologic conditions which they studied. The last investigators apparently did not use physostigmine in the eye or the standardized application of light according to the Engelhart technic.

METHOD

The plan of this investigation was to determine quantitatively the parasympathomimetic activity of the aqueous humor of human eyes prepared according to the method applied by Engelhart to rabbits. Each eye to be studied was prepared by the instillation of 1 drop of 1 per cent physostigmine salicylate into the conjunctival sac three times at ten minute intervals beginning one and one-half hours before operation. The purpose of administration of this drug was to inhibit the hydrolysis by cholinesterase of any acetylcholine formed. No other eye drops of any sort were used for twenty-four hours preceding the experiment, and no systemic medication was permitted. For one-half hour before the procedure the bright Hammer lamp of the operating room was focused on the subject eye, with winking permitted. In this way reflex stimulation of the parasympathetic nerves to the eye was produced. Anesthesia was obtained by retrobulbar injection of 2 cc of 4 per cent procaine hydrochloride. Preliminary studies on rabbits had shown that such a procedure did not produce a demonstrable change in the biologic effect of the aqueous humor of the eye. The conjunctival instillation of local anesthetic solutions was avoided, since their passage into the aqueous might influence the results of the bioassay. Approximately 0.1 cc of primary aqueous humor was obtained from each eye to be studied by paracentesis and aspiration with a hypodermic needle attached to a tuberculin syringe.

The biologic effect of each sample was tested within thirty minutes on the freshly prepared isolated heart of a spring or summer frog (*Rana pipiens*) according to the perfusion method of Straub.⁷ Fresh active hearts were employed, since such organs respond most readily to parasympathomimetic depressor effects. The preparations used in this study were usually found to be sensitive to acetylcholine chloride in dilutions of over 1:1,000,000,000. Before proceeding with each bioassay, it was necessary to prove the sensitivity of the isolated heart by testing its response to acetylcholine in such high dilutions. To preserve its activity, the aqueous was added without dilution to the Ringer solution in the cannula of the preparation. A kymographic record of the heart beat was made during each experiment. A quantitative estimation of the parasympathomimetic activity of each sample of aqueous humor was derived by comparison of its effect with that of known dilutions of acetylcholine chloride on the same preparation.

In the course of these bioassays of the aqueous, a delayed sympathomimetic augmentation of the heart beat was noted occasionally following the immediate parasympathomimetic depressor effect. Since this study was primarily concerned with cholinergic activity and these assay preparations were not sensitized for the controlled study of adrenergic effects, the latter were not considered at this time but will be the subject of further investigation.

6 Pletneva, N., Raeva, N., and Voronina, E. *Vestnik oftal* 13:462, 1938.

7 Sollmann, T. *Laboratory Guide in Pharmacology*, Philadelphia, W. B. Saunders Company, 1917, p. 190.

SUBJECTS

Samples of the aqueous humor of 40 human eyes were examined in this manner. Twenty of these eyes were from 19 persons without a history or signs of glaucoma. Three of these nonglaucomatous patients were, respectively, 23, 34 and 40 years of age, and the ages of the remaining 16 ranged from 50 to 74, with an average of 60 years. In this series of eyes without glaucoma, 4 were normal, 2 had pterygia, 8 had senile cataracts of various degrees of maturity, in 1 of which iridectomy had been done preliminary to extraction, and 6 had undergone extracapsular cataract extractions, with secondary discussions in 3 of them. In none of the eyes was any inflammatory reaction present at the time of our paracentesis. Four of these eyes had high degrees of myopia with associated myopic changes of the fundi. Four of the 19 patients in this group had diabetes mellitus, and in 3 of the eyes diabetic retinopathy was noted. Four other patients had advanced hypertension, and an associated retinopathy was seen in 1 eye. One patient had both hypertension and diabetes mellitus, with advanced retinopathy in the eye tested. A clinical impression was obtained of the atrophy of the iris present in each eye, this varied from none, in the more normal eyes, to an advanced degree, in some of the eyes in the aged and diabetic patients. No relationship was found between the results of the bioassay of the aqueous and the presence of systemic disease or the degree of uveal atrophy apparent in each eye.

The other 20 eyes tested were from 16 persons. Each of these patients presented a definite history and evidence of chronic simple glaucoma. The ages of these patients ranged from 44 to 79, with an average of 62 years. Included in this series of eyes were 5 in which the disease was clinically controlled with pilocarpine alone, 5 not treated surgically in which the glaucoma was not controlled with miotics, 3 in which simple iridectomy had been done, with subsequent control of the disease with supplementary use of pilocarpine in 1 eye and failure of control even with miotics in the other 2, and 7 in which the glaucoma was apparently controlled without miotics after treatment with filtering operations, from three months to ten years before. In the last group, that of eyes which had been successfully treated surgically, a trephination had been done on 1 eye, a modified Lagrange operation had been performed on 2 eyes and 4 eyes had benefited from iridencleisis.

In 4 of these 20 eyes recognized chronic simple glaucoma had been present for less than one year, and in 4 other eyes the disease had been known to exist more than ten years. In the entire series, the visual deficiency, cupping of the nerve head and field defects ranged from none to a pronounced degree, and atrophy of the iris was absent in some eyes and advanced in others. In short, every stage of clinically apparent chronic simple glaucoma was represented in this series of eyes. However, no eye was tested during an acute congestive exacerbation of the disease. The ocular tension as tested with fingers before paracentesis was seemingly elevated in some cases and within normal limits in others, without any apparently related effect on the results of the bioassay.

Five of the patients in this glaucomatous group had hypertensive vascular disease. Another had diabetes mellitus. The aqueous humor from the eyes of these patients did not vary in biologic activity from that of the other patients with glaucoma who did not have such systemic diseases.

RESULTS

In the series of 20 eyes without glaucoma the aqueous humor of 17 produced a definite parasympathomimetic depression in amplitude of

the heart beat. In 15 of these 17 eyes the intensity of this effect was found to be approximately equal to that of a similar amount of acetylcholine chloride in a dilution of 1:100,000,000. Figure 1 is the record of one such experiment. In the other 2 eyes in which a parasympathomimetic effect was produced the intensity was sufficient to cause diastolic standstill, an effect that could be duplicated by a similar amount of acetylcholine chloride in a dilution of less than 1:1,000,000. The 2 samples of aqueous that produced the latter effect were from a normal eye in a patient aged 23 and an eye with a senile cataract in a patient aged 70, respectively.



Fig 1—Kymographic record of the response of the isolated frog heart preparation to the aqueous humor from a nonglaucomatous eye with senile cataract. *A*, effect of 0.1 cc of acetylcholine chloride diluted 1:100,000,000; *B*, effect of 0.1 cc of aqueous humor from the nonglaucomatous eye.

In only 3 of the 20 eyes in this nonglaucomatous group did the aqueous humor show no parasympathomimetic activity. On 2 of these eyes extracapsular cataract extraction had been performed with subsequent discussion, so that the possibility of contamination of the sample of aqueous with vitreous must be considered. The third eye had a senile cataract. Two of these eyes had a high degree of myopia, and 1 of the patients had diabetes mellitus. Since all these conditions were also present in some of the eyes in the series of 17 the aqueous

of which produced parasympathomimetic effects, their occurrence in these 3 eyes cannot be considered as definitely related to the negative results of the bioassays of their aqueous

Enough aqueous humor was obtained from 7 of these nonglaucomatous eyes to permit the testing of two samples from each. After one-half the aqueous had been demonstrated to produce depression of the heart beat, 0.1 cc. of a 1:10,000 solution of atropine sulfate was added to the contents of the cannula and the second half of the aqueous tested. In each of these 7 samples complete inhibition of the parasympathomimetic

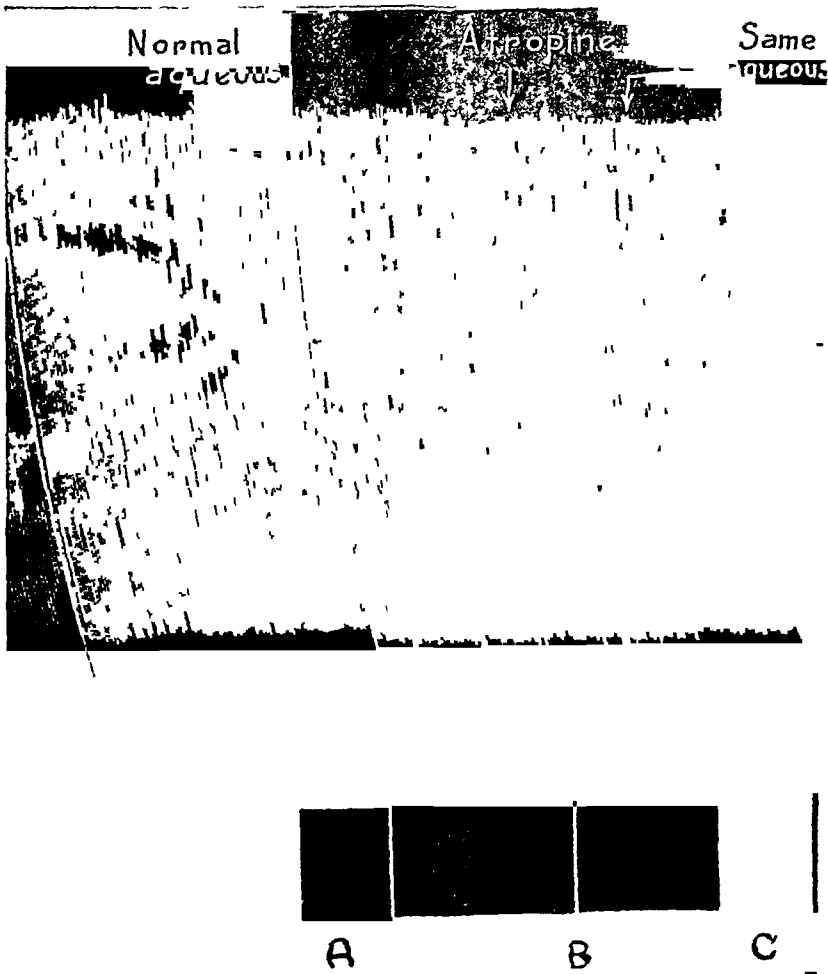


Fig. 2—Kymographic record showing inhibition by atropine sulfate of the parasympathomimetic effect of aqueous humor from a normal eye. *A*, effect of 0.08 cc. of aqueous humor from a normal eye, *B*, effect of the addition of 0.1 cc. of a 1:10,000 solution of atropine sulfate to the perfusion fluid, *C*, subsequent effect of 0.08 cc. of the same sample of aqueous humor as that shown in *A*.

effect previously noted occurred. Figure 2 is the record of one of these experiments. Since it is characteristic of the pharmacologic effect of acetylcholine that it is inhibited by atropine, this demonstration strongly indicates that the parasympathomimetic agent in the aqueous is similar to, or identical with, acetylcholine.⁸

⁸ Chang, H. C., and Gaddum, J. H. *J. Physiol.* 79:255, 1933.

The samples of aqueous humor obtained from the 20 eyes with chronic simple glaucoma were studied in an identical manner. In 15 samples no parasympathomimetic effect whatever was recorded. Figure 3 is the record of a bioassay of aqueous humor from an eye with chronic simple glaucoma. The aqueous humor of the remaining 5 eyes in this series produced a very slight depression of the heart beat, which on quantitative comparison was found in each case to be less than that produced by an equivalent amount of acetylcholine chloride in a dilution



Fig 3—Kymographic record of the response of the isolated frog heart preparation to aqueous humor from an eye with uncontrolled chronic simple glaucoma. *A*, effect of 0.1 cc of acetylcholine chloride diluted 1:100,000,000, demonstrating the sensitivity of the preparation, *B*, effect of 0.1 cc of aqueous humor from an eye with chronic simple glaucoma.

of 1:1,000,000,000. These 5 eyes included 2 the tension of which was well controlled with miotics and which showed only minimal impairment of the visual fields and minimal visual defects, 1 in which the tension was controlled with pilocarpine after previous iridectomy but which showed advanced changes in the fields and advanced visual defects, 1 in which the glaucoma was controlled without medication after

iridencleisis and in which only moderate functional impairment had occurred, and 1 not operated on the tension of which was not reduced with miotics and which showed advanced glaucomatous damage. Both eyes of 4 patients with bilateral chronic simple glaucoma were included in this series. In every instance the results of the bioassay were identical in the two eyes of the same subject.

Since parasympathomimetic activity was detectable in the aqueous of only 5 of the 20 eyes in this series, and since even in these eyes it closely

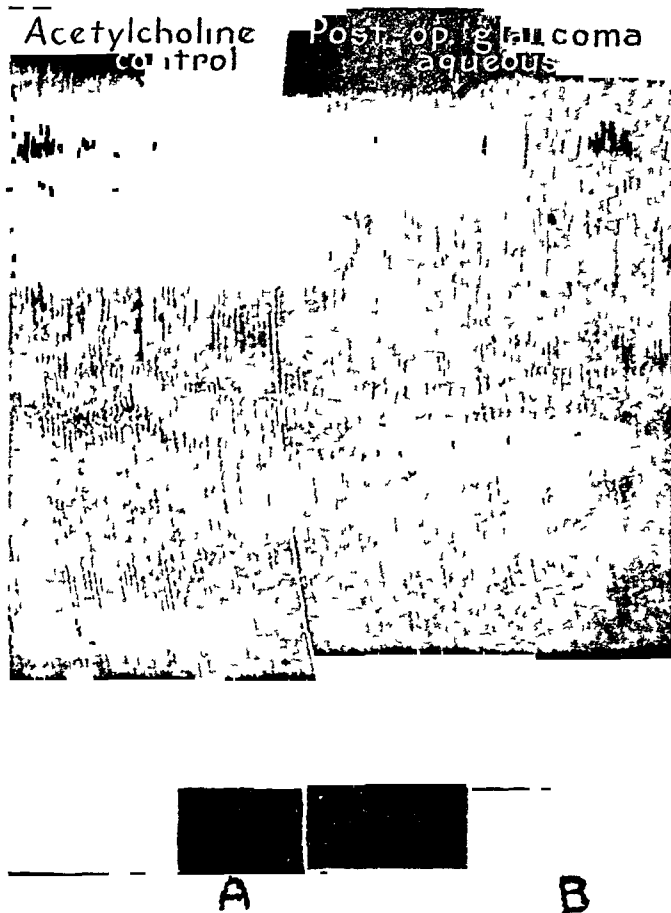


Fig 4—Kymographic record of the effect of the aqueous humor from an eye with chronic simple glaucoma which had been successfully controlled by iridencleisis seven months before. A, effect of 0.1 cc of acetylcholine chloride diluted 1:100,000,000, B, effect of 0.1 cc of aqueous humor from the eye with chronic simple glaucoma which had been successfully treated by operation.

approximated the limit of sensitivity of our bioassay preparation, no definite conclusions could be drawn with this method concerning a possible relation between the stage of the disease in each glaucomatous eye and the amount of parasympathomimetic activity present in its aqueous humor. It should be noted, moreover, that the absence of biologic effect of the aqueous on these preparations did not necessarily indicate a complete lack of parasympathomimetic activity in that fluid, but showed only that the amount present was too small to be detected.

with this method of assay. However, it is apparent that in no instance did the aqueous humor from any of the 20 eyes with chronic simple glaucoma cause a parasympathomimetic effect as intense as that produced by aqueous from 17 of the 20 nonglaucomatous eyes previously described.

As previously noted, in the series of eyes with chronic simple glaucoma 7 were included that had undergone filtering operations some time before, and in each of these eyes surgical intervention had been so successful that the disease was considered clinically controlled without further use of miotics. Nevertheless, the aqueous humor from 6 of these eyes produced no effect on the frog heart, and that of the remaining eye caused only a slight parasympathomimetic effect, equivalent to that of acetylcholine chloride in a concentration of less than 1 1,000,000,000. Figure 4 is the record of the effect of the aqueous from 1 of these eyes which had been successfully operated on for chronic simple glaucoma. In 1 of the 7 cases the opportunity was afforded to test the aqueous before operation, when tension was persistently abnormally high, and, again, three months after successful iridencleisis had reduced the tension to normal. The results of these two bioassays were exactly alike in failing to disclose any parasympathomimetic activity in the aqueous humor. It would appear, therefore, that filtering operations for the alleviation of chronic simple glaucoma, even when successful in clinically controlling that condition, do not affect the deficiency of parasympathomimetic activity of the aqueous humor which is apparently associated with that disease.

COMMENT

The diminution in parasympathomimetic activity of the aqueous humor that has thus been shown to occur in eyes with chronic simple glaucoma may be due either to an actual decrease in the amount of acetylcholine usually present in the aqueous of nonglaucomatous eyes or to inhibition or counteraction of the normal amount of acetylcholine by substances pathologically present. Experiments are now under way to clarify this point.

Since appreciable degrees of cholinergic activity were found present in the aqueous of eyes with a fairly wide variety of nonglaucomatous conditions, and since such cholinergic activity apparently was significantly reduced consistently only in eyes with chronic simple glaucoma, it seems likely that this parasympathomimetic deficiency is related to some physiologic disturbance specific for the latter disease. The question arises whether this reduction in cholinergic activity is an etiologic factor in the development of chronic simple glaucoma or simply the result of the presence of that disease.

It was previously pointed out that the administration of parasympathomimetic drugs has a stabilizing effect on the abnormal lability of

ocular tension that is present in eyes with chronic simple glaucoma. Such drugs also frequently provide therapeutic relief from the abnormally high intraocular pressure present in that disease. These facts strongly suggest that naturally occurring cholinergic substances play a role in the normal regulation of ocular tension. The deficiency of such substances in the aqueous of eyes with chronic simple glaucoma is therefore probably etiologically related to the abnormal intraocular pressure that occurs in that disease. Only in this way can one explain the therapeutic result of administering parasympathomimetic drugs, which in effect relieves that deficiency to some degree.

It is obvious that this demonstration of altered biologic activity in the aqueous humor of eyes with chronic simple glaucoma does not in itself clarify the basic nature of that disease. However, it offers experimental evidence of a physiologic aberration the presence of which was hitherto only suspected, and further investigation of which may throw more light on the problem of regulation of ocular pressure and the therapy of chronic simple glaucoma.

SUMMARY

A method of bioassay is described whereby a quantitative approximation of the parasympathomimetic activity of the aqueous humor of human eyes may be derived.

In 17 of 20 nonglaucomatous eyes with various noninflammatory pathologic conditions, an appreciable parasympathomimetic effect was demonstrable in the aqueous humor.

In each of 7 eyes in which the aqueous humor could be further studied, this cholinergic activity was found to be due to the presence of acetylcholine.

In 15 of 20 eyes in various stages of chronic simple glaucoma, no such parasympathomimetic activity could be demonstrated in the aqueous humor. In the remaining 5 eyes in this series, the intensity of the parasympathomimetic activity present was significantly lower than that which occurred in the aqueous of the 17 nonglaucomatous eyes which produced cholinergic effects.

This relative deficiency of parasympathomimetic activity of the aqueous humor in eyes with chronic simple glaucoma was not altered by the successful treatment of the disease with various filtering operations.

There is evidence that this relative deficiency in parasympathomimetic activity of the aqueous of eyes with chronic simple glaucoma is related to the faulty regulation of intraocular pressure which occurs in that disease.

Miss Mary Carsten gave technical assistance in this work.

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SENSORIAL RETINAL RELATIONSHIP IN CONCOMITANT STRABISMUS

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(Concluded from Page 533)

V ORIGIN OF ANOMALOUS CORRESPONDENCE

Nothing is known about the mechanism which brings about the loosening of the normal sensorial relationship and the revaluation of the spatial values of the retina of the deviated eye. For the time being, one is entirely dependent on speculation in this matter. However, any consideration of the problem must take account of the following facts: (a) Anomalous correspondence may be observed even in cases of extreme amblyopia of the deviated eye, and (b) it is the prolonged simultaneous stimulation of the fovea of one eye and of an eccentric element of the retina of the other eye that leads in some way to the establishment of anomalous correspondence.

Deeply rooted anomalous correspondence may be observed in cases of extreme amblyopia. For instance, I have seen a student with a congenital, partly absorbed cataract. After this cataract was removed by needling, vision in that eye—in spite of a clear pupillary area and a normal fundus—was never better than 20/200 with correction, most of the time the vision was considerably worse. Nevertheless, and in spite of the fact that he wore no correction for his aphakic eye, the patient when examined one and a half years after the operation for the cataract showed in the double image and after-image tests an anomalous retinal correspondence adapted to his divergent squint of 18 arc degrees.

The teleologic explanation of anomalous correspondence, so often cited in this paper, that it is an attempt of the organism to restore binocular vision on the basis of usage of the eyes, would appear to fall down entirely in the light of this and similar observations. This patient could not have derived any conceivable benefit from the acquisition of a common visual direction between the fovea of the fixating eye and a peripheral element of the retina of the deviated eye. Still less could it have been brought about by a unifying act of attention, as has been stated by some authors (Linksz,⁵⁰ Mann⁵⁶), since it is most unlikely that the patient would have paid attention to the extremely faint images

⁵⁶ Mann, D. S. Orthoptic Treatment of Anomalous Projection, *Brit J Ophth* 27:215, 1943

received by his left eye. For the same reason, Hering's⁵⁷ explanation cannot apply. He expressed the belief that the experience with the relative position of objects in the field of view and their localization relative to the head and body of the patient acquired by frequent alternation eventually leads to the acquisition of different visual directions by the two foveas.

Yet anomalous correspondence adapted to the angle of squint did exist in this patient. One must assume that it came about by a physiologic process which takes place as long as the proper conditions of stimulation are given—a process which again shows the inescapable tendency of the organism to unify the monocular into binocular excitations.

An attempt to explain this physiologic process was made by Sachs⁵⁸. This author assumed that two processes are taking place concurrently. The foveas of a squinting patient receive two different images. The physiologic preponderance of the fixating fovea leads to the neglect of the image received by the fovea of the deviated eye. As a consequence, the physiologic rivalry between the foveas disappears. At the same time, the eccentric retinal element on which the fixation point is imaged becomes increasingly effective in the binocular act, rivalry between it and the fixating fovea develops, and a common visual direction is established. Bielschowsky^{31a} did not subscribe to this theory, he maintained that in order to attain rivalry the disparate elements first must have a common visual direction. This is undoubtedly true for normal physiologic rivalry. But could not the rivalry between the fixating fovea and the eccentric retinal element of the deviated eye be of a type different from the normal?

Tschermak-Seysenegg,³⁰ Bielschowsky,^{31a} Braun,²⁴ Harms⁵⁹ and, particularly, Travers²¹ made interesting and pertinent experiments concerned with suppression and functional scotomas associated with strabismus which reveal a relationship between amblyopia, suppression and anomalous correspondence. According to Travers' observations, there can always be mapped out by perimetric methods in the deviated eye a region of suppression corresponding on the Bjerrum screen to the retinal area which has a common visual direction with the fovea of the fixating eye. Thus, in cases of normal retinal correspondence this area on the screen has as its approximate center the line of direction of the fovea of the deviated eye, in cases of anomalous retinal correspondence this center

⁵⁷ Hering, E. Ueber die anomale Lokalisation der Netzhautbilder bei Strabismus alternans, *Deutsches Arch f klin Med* **64** 17, 1899.

⁵⁸ Sachs, M. Ueber das Alternieren der Schielenden, *Arch f Ophth* **48** 443, 1899.

⁵⁹ Harms, H. Ort und Wesen der Bildhemmung bei Schielenden, *Arch f Ophth* **138** 148, 1938.

is represented by the line of direction pertaining to the eccentric retinal element of the deviated eye which has a common visual direction with the fovea of the fixating eye

Both Harms and Travers agreed that this regional suppression is intimately associated with anomalous correspondence. Harms went so far as to claim that to establish the presence of regional suppression is equivalent to demonstrating that there is anomalous correspondence.

Travers maintained that the larger the angle of anomaly, the greater is the area of suppression. He formulated the following theory of the origin of anomalous correspondence.⁶⁰ In the nonfixating eye, first the macular area is suppressed to avoid diplopia, then the eccentric area on which the fixation point is imaged is suppressed to avoid confusion (simultaneous perception of different object points in the same visual direction). This suppression causes the object point which is imaged on the macula of the deviated eye to be perceived in the monocular visual direction of the fixating eye, and this gradually alters the power of discriminating direction in the deviated component of the binocular visual field. By a succession of processes of suppression and readjustment of the visual directions there finally are established a definite area of suppression and an anomalous correspondence adapted to the angle of squint.

This theory sounds plausible, but it is not borne out by clinical experience. I have never observed gradual changes in the angle of anomaly.⁶¹ Nevertheless, although future investigations must determine the mechanism by which anomalous correspondence is established, these will probably have to be conducted along the lines which were first suggested by Sachs forty-five years ago, and along which Travers and Harms have lately worked.⁶²

60 Travers, T à B. The Origin of Abnormal Retinal Correspondence, *Brit J Ophth* 24 58, 1940

61 E. E. Cass (Anomalous Retinal Correspondence, *Tr Ophth Soc U Kingdom* 58 276, 1938) stated explicitly, however, that "it is curious to note during squint training that the false point moves nearer and nearer the macula as macular-binocular vision improves."

62 Travers' findings²¹ are as yet by no means fully explained. Most of them do not directly relate to the topic of this paper and will therefore not be discussed here. I wish only to point out that Travers concluded from his results that anomalous retinal correspondence cannot lead to a useful, though inferior, type of binocular vision, as is often assumed. This is, in his opinion, precluded by the regional suppression in anomalous retinal correspondence. Travers' conclusion can at best relate to the cooperation between the macula of the fixating eye and the eccentric element of the deviated eye. There is, however, as a rule little suppression in the other regions of the binocular field (Harms⁶⁰ and others), and I¹³ was able to show that there may be a high degree of binocular cooperation with anomalous correspondence in peripheral retinal areas when the central area of one eye is suppressed. A case of this type is also reported in the present

The findings of the modern school of psychophysiology of vision will also have to be considered, and its observations and methods may possibly help to furnish a clue to the solution of the problem. A further development of Lorente de Nó's speculations³⁹ about the point to point relationship of the retinas may be helpful, and it must be kept in mind that Tschermak-Seysenegg, Braun and other representatives of the nativistic school stated the belief that a certain deficiency in the *Anlage* of the normal correspondence is necessary for anomalous correspondence to come about.

VI CRITICAL REVIEW OF THE LITERATURE OF THE LAST TWO DECADES CONCERNED WITH ANOMALOUS CORRESPONDENCE

As was pointed out by Wheeler,⁶³ two periods in the literature on anomalous correspondence may be distinguished. The first period, extending roughly to 1925, began about 1895, although occasional attention had been given to the subject prior to that date. This is the period in which the most important fundamental papers appeared, written or inspired largely by physiologists.

During this first period the rank and file of the ophthalmologists did not even suspect the existence of anomalous correspondence. Not until it was recognized by the ophthalmologists at large that strabismus is a sensory as well as a motor disturbance and until interest in orthoptic treatment became more widespread was the subject taken up again. For the past twenty years a rather voluminous literature on anomalous correspondence has sprung up, although, strangely, some of the most recent and most widespread monographs on strabismus do not even mention it.

The present section is concerned with a critical survey of the literature of the second period. Completeness is attempted, but not all papers in which anomalous correspondence is merely mentioned are cited. Only the more important papers are discussed in some detail. A number of papers which have been referred to in previous sections will not be discussed again.

A great deal of confusion reigns in the literature of the last twenty years on anomalous correspondence. It can be traced almost invariably to a lack of knowledge of the literature of the first period and to a lack of understanding of the basic physiologic processes involved. It will

paper (case 22). Tschermak-Seysenegg³⁰ discussed in detail the binocular visual act in anomalous correspondence. He stated that there is no doubt that the possibility of binocular mixture and binocular contrast exists in spite of the sensorial inequality of the two eyes. Both eyes participate in the binocular visual field even in anomalous correspondence, though there is to some extent a suppression of the visual impressions of the squinting eye.

63 Wheeler, M. C. History of Orthoptics, *Am J Ophth* 25:569, 1942.

become apparent in the course of the discussion that two main misconceptions are at the root of the confusion. The old projection theory, though in general abandoned in its original form, still prevails in the minds of most authors, and no difference is made between absolute, or egocentric, spatial localization and relative localization, to the latter of which the concept of anomalous correspondence exclusively refers.

This survey will be divided into three parts. The first deals with the theory of anomalous correspondence, the second, with monocular diplopia and binocular triplopia, and the third, with anomalous correspondence as it relates to orthoptic treatment.

I THEORY OF ANOMALOUS CORRESPONDENCE

In 1931 and 1932 there were published posthumously two articles by Duane⁶⁴ which elaborate the contents of an earlier paper by the same author⁶⁵. These papers give a clear presentation of the projection theory as modified by Duane and are helpful in explaining much that has been written subsequently on anomalous correspondence.

According to Duane, the visual impressions are projected or referred to a definite portion of space outside the body, in monocular as well as in binocular vision. In binocular, as in monocular, projection visual and postural elements aid in the localization. The visual element helps one localize an object through the impression produced by the retinal image. In this respect binocular is like monocular projection, except for the added sensation of depth when the retinal images are not quite identical.

Duane stated that the postural elements are the sensations derived from the movements of the head, the conjugate movements of the eyes and, in binocular vision, the sensations derived from convergence. The sensations coming from the muscles of the head tell one whether the face is directed straight forward or not. The eyes are made aware of their movements by the muscle sense. It is this awareness which produces spatial localization. The lateral and vertical conjugate movements of the eyes inform one as to whether the visual plane is horizontal or tilted and whether the object of fixation is straight ahead, to the right or left, or above or below. The sensations arising from the convergence effort determine whether one object appears nearer or farther away than another.

There is, however, an essential difference between monocular and binocular projection. In the former, each eye projects as if it were in its own place, and in the latter, as if each eye were transferred to the

64 Duane, A. (a) *Binocular Vision and Projection*, Arch Ophth 5 734 (May) 1931, (b) *Diplopia and Other Disorders of Binocular Projection*, *ibid* 7 187 (Feb) 1932.

65 Duane, A. *Projection and Double Vision. Some New Viewpoints*, Arch Ophth 54 233 (May) 1925.

midline In monocular vision each eye projects with reference to its own axis, and in binocular vision, with reference to the midline, or "bivisual line", i. e., binocular projection may be conceived as performed by a single cyclopean eye, or *binoculus* This change in the line of reference is proved by the fact that in physiologic diplopia the double images are projected not to the plane of the fixation point but to the plane in which the object lies which is seen double

Duane thus showed that the old projection theory is unable to explain physiologic diplopia—which is one of the reasons that Javal and Hering, who were not mentioned by Duane, rejected the projection theory—and accepted the concept of the cyclopean eye However, he still adhered to the projection theory Since it does not in itself explain binocular spatial localization, the concept of the "muscle sense" of the eye, introduced by Nagel, the founder of the projection theory, is used to explain both egocentric (at a distance from, or above or below, or to the right or left of, the observer) and relative localization, which are not distinguished

Duane claimed further that convergence and conjugate movements produce sensations which cooperate in binocular projection and explain physiologic diplopia This is also supposed to explain pathologic diplopia In esophoria, for instance, both eyes tend to converge on a point nearer than the fixation point This excess of convergence is compensated for by an impulse for lateroversion of one eye, accompanied with a conjugate movement of the other eye Thus, the convergence is reduced in one eye until the eye comes to be directed to the fixation point, while the other eye converges even more than before Since the two eyes are subject to an equal convergence effort in the case of an ocular deviation, just as in the case of binocular fixation, all images formed on the retina of either eye are projected as though the two eyes were united in the binoculus and their visual axes coincided with the bivisual axis Diplopia produced by prisms or by paralyses of the ocular muscles are explained analogously

Before giving Duane's views on anomalous correspondence, a significant paragraph, entitled "Diplopia Always Due to False Projection,"^{64b} will be reproduced in its entirety

It must be noted that binocular diplopia, whether physiologic or pathologic, is always the result of false projection In monocular vision the eye almost invariably projects correctly, the combination of visual and postural impressions enables it to do this In binocular vision the two eyes, if acting in a normal way, project correctly the object looked at with even more accuracy than in monocular vision They also project correctly a few outlying objects, which form images on corresponding points, or which at any rate occupy the horopter But all other objects are projected out of their true place, and the same is true of all objects seen by the deviating eye The false projection in both cases is due to the preponderance of the postural expressions derived from convergence over those derived from conjugate movements, i. e., it is due to the fact that when one looks

with both eyes one locates objects with reference to the midline instead of with reference to the visual axes of the eyes themselves

If the postural impulses derived from conjugate movement chance to reassert themselves and partially or wholly to replace those derived from convergence, the diplopia diminishes (becomes incongruous) or disappears (suppression)

The last sentence contains the essence of Duane's concept of anomalous correspondence. The interplay between the monocular type of vision (projection by conjugate impulses) and the binocular type (projection by convergence impulses) explains "incongruous diplopia" (which exists when the deviation found by the objective tests differs in amount from that shown by subjective tests) and "suppression" (which is the terminal stage of incongruous diplopia and is often associated with it). In ordinary diplopia the deviating eye, dominated by convergence impressions, locates its visual axis in the midline. When the deviated eye is wholly under the influence of conjugate impressions, it locates its visual axis where it actually is, but since the image of the fixation point is less distinct it will be suppressed. If the reversion to the monocular type of vision is not complete, the eye, being under the influence of both convergence and conjugate impulses, locates its visual axis along some intermediate line.

In discussing Duane's theory of spatial localization, it must be said that with the introduction of the cyclopean eye the projection theory is no longer applicable and becomes devoid of meaning.¹⁴ The introduction of the "muscle sense" does not give it meaning since it has long since been established that there is neither anatomic⁶⁶ nor physiologic evidence (von Helmholtz,¹¹ Hering,^{9c} Hofmann,¹¹ Tscherning,⁶⁷ Irvine and Ludvigh⁶⁸) for a muscle sense of the eyes of such a highly differentiated nature that it could account for all visual spatial orientation. The theory breaks down completely when it is applied to the explanation of anomalous correspondence after successful operation on the ocular muscles which has restored the balance of the conjugate movements. The paradoxical diplopia which is so often, and often so persistently, observed cannot be accounted for on the basis of the "muscle sense."

Only the theory of retinal correspondence on the basis of common subjective visual directions offers an unequivocal explanation for all phenomena observable in normal binocular vision and in pathologic cases.

Duane's theory may be considered obsolete, and I would not have given it such detailed presentation if it were not for the fact that similar

66 Irvine, S. R. Histology of Extra-Ocular Muscles, Arch Ophth **15** 847 (May) 1936

67 Tscherning, M. Physiologic Optics, translated by C. Weiland, Philadelphia, Keystone Publishing Company, 1900

68 Irvine, S. R., and Ludvigh, E. J. Is Ocular Proprioceptive Sense Concerned in Vision? Arch Ophth **15** 1037 (June) 1936

views, which are the source of much confusion,⁶⁹ still crop up in the orthoptic literature on the subject of anomalous correspondence

This is evident also in a paper by Verhoeff,¹⁰ in which he wished to correct what he believed to be prevalent misconceptions concerning certain visual phenomena associated with strabismus, particularly as regards anomalous retinal correspondence, or, as he termed it, anomalous projection

It is difficult even for one well versed in the subject to follow Verhoeff's paper. For one not intimately acquainted with the subject it is probably impossible to understand it. Yet Verhoeff came to such sweeping conclusions regarding anomalous correspondence that his paper commands close attention

Verhoeff began his paper by defining corresponding retinal points and stated that many definitions have been attempted, some of which are evidently inaccurate while others are inadequate or ambiguous. I do not know what authorities Verhoeff consulted about this definition, or where he found the two definitions which he quoted as examples, since he gave no references. But surely they were not given by the best authors

According to the first definition, "corresponding retinal points are retinal points which are projected to the same place in space." This definition is certainly erroneous. It is erroneous, first, because "retinal points" cannot be projected into space, but only visual impressions, second, because visual impressions are not projected into (objective) space but are localized in (subjective) visual space, and, third, because visual impressions produced by simultaneous stimulation of corresponding retinal elements do not of necessity have to be localized at the same place in subjective space. Verhoeff objected to this definition because it "does not include the case in which an image on one retina is projected 6 inches (15 cm) away and an image in the corresponding area is projected 6 miles (9,656 meters) away." This objection is not valid, since the concept of retinal correspondence does not imply depth localization, but pertains only to the relative localization in the horizontal and vertical

69 To cite one example, Hoorens⁴⁵ stated "The majority of the classic writers give no plausible explanation of false projection. I believe that I can explain the majority of cases in the following way. False projection is found mostly in patients with alternating strabismus. The alternating strabismus continues after the operation and is so rapid that the patient thinks he can see two lights at the same time. But since after the operation the internal rectus muscle has to exert less effort to straighten the eye than before the operation, the patient experiences the sensation that the object seen by the strabismic eye is located more to the nasal side. He therefore projects it more to the nasal side, i. e., sees it in crossed diplopia."

As another example, see Pascal, J. I. Visual and Orthoptic Training, *Am J Ophth* 17:801, 1934

dimensions The distance at which stimuli are localized cannot enter into the definition of retinal correspondence, but only the direction in which they are seen is concerned

The second definition quoted by Verhoeff, "that corresponding retinal points are retinal points that are projected in the same direction," comes, therefore, closer to the truth, although, again, neither "retinal points" nor, for that matter, visual impressions are "projected" in any direction Verhoeff stated that this definition does not distinguish between "normal and anomalous projection," which he endeavored to prove in his paper

Verhoeff then gave his own definition of corresponding retinal points Using in schematic and slightly modified form the old experiment of Hering by which he proved the existence of common visual directions, Verhoeff introduced a new terminology The line connecting the center of an object point with its image on the retina he called a "visual axis" He then stated—without proving it in the text or in the diagram—that objects lying on certain "visual axes" of the two eyes are seen to lie on an imaginary line, which he termed a "binocular visual axis" Corresponding retinal points were defined as the retinal optical terminals of corresponding visual axes

An analysis of this definition shows that it is by no means really new, but its formulation is such that it confuses, rather than clarifies, the concept of corresponding points What Verhoeff termed the "visual axis" is nothing other than what is known as the "line of direction" This line is simply a geometric construction which determines which retinal element will be stimulated By no stretch of imagination is it possible to conceive that any two "corresponding visual axes" could coincide or appear to coincide—not even "as visualized from their respective eye" Not even the strictest adherents of the projection theory have ever claimed that the lines of direction coincide, they have only claimed that the visual impressions are projected outward along the lines of direction (i e., Verhoeff's visual axes)

How and why these visual axes coincide, Verhoeff did not say But the gap is easily filled if the concept of the subjective visual directions, which Verhoeff did not recognize, is introduced His definition, then, in essence, becomes identical with the classic one, according to which corresponding retinal elements are those elements which have a common subjective visual direction

What has been pointed out here is, to my mind, not a play on words, it goes to the essence of the binocular visual process A clear understanding of these processes requires a clear terminology, and, vice versa, a clear terminology makes for clear understanding This has been emphasized time and again by Lancaster⁶

The main point which Verhoeff made in his paper is that in "anomalous projection" there are no "corresponding visual axes" and that it

is, therefore, a "type of binocular projection without retinal correspondence" He has found that not one retinal element but a large retinal area of the squinting eye may have temporarily "corresponding visual axes" with the principal visual axis of the fixating eye and that there is thus in "anomalous projection" a type of retinal correspondence which is not fixed but variable The variability and instability of the sensorial retinal relationship in anomalous correspondence is a well known phenomenon, emphasized by all good writers, it is an essential characteristic of the anomalous retinal relationship and has led Tschermak to pertinent criticism of the terminology, as will be seen in the last section of this paper Harms even stated that this variability may be an imperfect substitute for fusional movements

The question, however, is how Verhoeff showed this instability and whether it justifies his sweeping conclusions Verhoeff used two methods to prove his point One was the "subjective cover test," in which the patient has to state whether the fixated object point, situated at 6 meters, appears changed or unchanged in its position when a cover is quickly transferred from one eye to the other The other he described as follows The patient fixates (either at 6 meters or at 10 cm) an object point with one eye Other objects are then placed anywhere along the visual axis of that eye, and the eyes are alternately covered Again, the various object points appear "in the same place in space no matter from which eye they are seen" Thus, "although an object is moved along a monocular visual axis of one eye and the position of its retinal image in the other eye constantly changes, the two images continue to correspond"

There are various objections, possibly of minor importance, which could be raised to these experiments, which are described only in principle The principal objection, however, that they do not test retinal correspondence at all, is valid in any case Aside from the fact that the condition of the sensorial retinal relationship can be determined only by simultaneous stimulation of selected retinal areas, Verhoeff's tests relate to the absolute, not the relative, localization And these two, as has been pointed out repeatedly in this paper, must be strictly separated The condition of the sensorial retinal relationship is determined not by the localization of an object point in subjective space relative to the coordinates of this space and to the subjective coordinates of the observer's head and body, but by the localization relative to each other of stimuli reaching simultaneously specified areas of the two retinas Verhoeff's criticism of the after-image test, that the "criteria of distance are inadequate for each eye," is therefore without any foundation

That Verhoeff did not distinguish absolute and relative localization is borne out by the fact that throughout the paper he spoke of "correct" and "incorrect anomalous projection" He stated explicitly that "since the term anomalous as applied to binocular projection refers only to the

type of projection, it carries no implication as to the correctness of the projection. Obviously, there may be anomalous correct or incorrect projection, depending on the monocular projection."

At the bottom of this confusion of egocentric and relative localization is the fact that Verhoeff espoused the projection theory of spatial localization. In a significant passage, Verhoeff stated

In the case of retinal correspondence, monocular depth criteria (such as size) have nothing to do with determining the direction of any monocular or binocular visual axis, that is to say, with determining the apparent angular direction of any object. In the case of anomalous projection, however, monocular depth criteria derived from the squinting eye, even when binocular criteria are removed by means of a suitable screen, can determine the apparent direction of an object as seen from only that eye in binocular vision. As concerns any object well within the binocular field, the visual axis of a retinal image in the squinting eye intersects innumerable visual axes of the fixing eye. To which of these intersections the image is projected, and hence in binocular vision along which axis of the fixing eye it is projected, monocular depth criteria derived from the squinting eye can determine. Thus whether *A* and *B* are projected to their actual locations or to the crossing point *P* can depend solely on monocular depth criteria. This analysis reveals one of the fundamental distinctions between the projection of a person with fixed retinal correspondence and that of a person with anomalous projection.

I believe this lengthy analysis has shown that there is nothing in Verhoeff's paper which would compel one to accept his statement that there are "no corresponding visual axes" in anomalous retinal correspondence or to justify his criticism of the expression "anomalous correspondence adapted to the angle of squint," made on that basis. The concept does not have to be relinquished that in many squinters a common visual direction between *de norma* disparate retinal elements can be shown to exist at a given time and under the test conditions. Even though this relationship may not have the stability of the normal correspondence, it is in some cases stable enough to persist quantitatively over many years, even if the relative position of the eyes is changed by operation. These cases, together with the different types of cases in which normal and anomalous correspondence coexist, afford the most conclusive clinical evidence against Verhoeff's point of view. He recognized this, of course, and stated that "no doubt these [cases of post-operative triptopia] are usually due to persistence of the old anomalous projection, now incorrect, along with the development of new and correct projection." How an anomalous projection which allegedly consists in an absence of "binocular visual axes" can persist after an operation which has straightened the eyes and produce a monocular diplopia in which one image is at a distance corresponding to the old angle of squint is entirely inexplicable, and Verhoeff made no attempt to explain it. Nor is it clear how this and similar phenomena could at all be interpreted on the basis of a theory according to which spatial localization occurs by projection along the lines of direction.

The theory of common visual directions also explains some interesting observations on the ϕ phenomenon in patients with strabismus, which were published by Verhoeff in 1940⁷⁰

The ϕ phenomenon, so named by Wertheimer,⁷¹ consists in an apparent movement which occurs when different groups of retinal elements are successively stimulated in a specified way and at specified time intervals. "Moving" advertising signs have familiarized every one with the phenomenon. It occurs not only in monocular and binocular vision, but also when the stimuli are successively presented to different regions of the retinas of the two eyes. Verhoeff had the ingenious idea to test the ϕ phenomenon in patients with convergent and divergent strabismus by exposing a luminous target for one-twentieth second first on the fovea of one eye and then an identical target on the fovea of the other eye. The two targets were placed at 60 cm from the observer and separated by his angle of squint. In these circumstances, an observer with normal retinal correspondence should not see a movement, but if he has anomalous correspondence a movement should occur in accordance with the angle of anomaly.

Verhoeff found that the ϕ phenomenon was indeed readily elicited in all 13 patients whom he examined. In addition, he performed an experiment on a patient with facultative divergent squint in which he placed the luminous targets so that the one seen by the left eye fell 4 arc degrees temporal to the left fovea and the one seen by the right eye fell 8 arc degrees temporal to the right fovea, both when the patient's eyes were dissociated and when he fixated binocularly. In the first instance the two luminous targets were to the right of a rod placed at 60 cm from the patient in his median plane, in the second instance the target seen by the right eye was moved to the left of the fixation rod. The target *A* (seen by the left eye) was always illuminated first. Both when the eyes of the patient were dissociated and when he fixated binocularly, an apparent movement from *A* to *B* (seen by the right eye) occurred, only in the first case the movement was from left to right, in the second, when target *B* was to the left of the fixation rod, from right to left.

Verhoeff did not explain the result of this experiment but used it as a basis for a short criticism of Wertheimer's theory of the ϕ phenomenon. Actually, the explanation is quite simple and in no way affects Wertheimer's theory. The fact, stressed by Verhoeff, that the external criteria were interpreted correctly in each instance is of no significance.

⁷⁰ Verhoeff, F. H. *Phi Phenomenon and Anomalous Projection*, Arch Ophth **24** 247 (Aug) 1940.

⁷¹ Wertheimer, M. *Experimentelle Studien über das Sehen von Bewegungen*, Ztschr f Psychol **61** 161, 1912.

The ϕ phenomenon is based on the successive stimulation of retinal elements having different visual directions. Verhoeff did not recognize the importance of the visual directions, which is why the results of the experiment appear puzzling. Assuming that the patient had an anomalous retinal relationship when his eyes were dissociated, the visual direction of the retinal point, b , on which the image of target B falls would have approximately the visual direction β . In the cyclopean eye α would be to the left of β , and the successive stimulation of a and b would produce an apparent movement from left to right (fig 9A). When the patient fixated binocularly, he used presumably normal correspondence, as happens so often in cases of facultative divergent strabismus,⁷² and the visual direction of α in the cyclopean eye would now be to

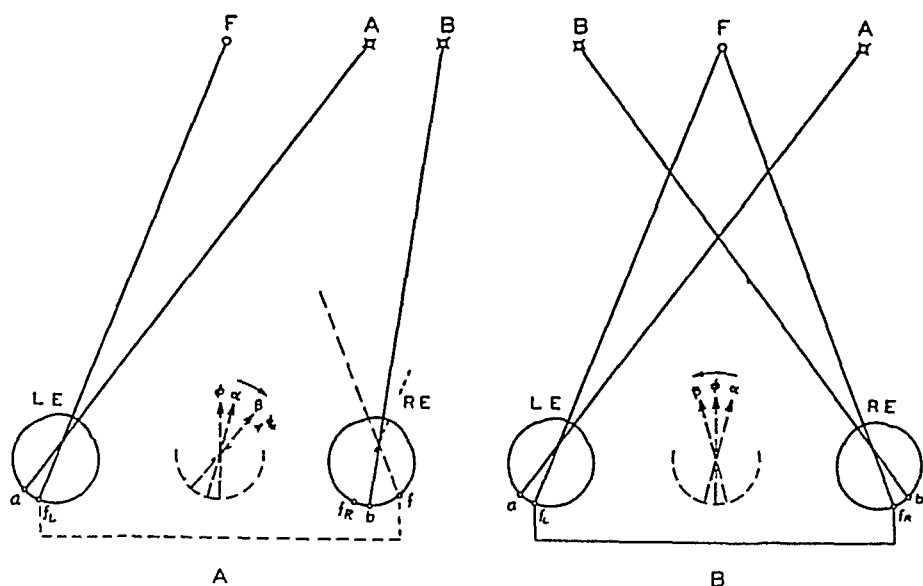


Fig 9—Diagram illustrating a possible explanation of Verhoeff's ϕ phenomenon experiment in a case of facultative divergent strabismus

the right of β (fig 9B). Consequently, the successive stimulation of a and b would produce an apparent movement from right to left. This would not occur if the patient should continue to localize according to his anomalous correspondence while fixating binocularly. The position in space of the targets does not influence the direction of the movement, it is determined by the visual directions of the stimulated elements.

Verhoeff's observations would thus confirm beautifully the theory of retinal correspondence adopted in this article. Unfortunately, Verhoeff's paper is very short and lacks much pertinent information. For

72 Burian, H. M. Motility Clinic. Intermittent (Facultative) Divergent Strabismus, Its Influence on Visual Acuity and the Binocular Visual Act, *Am J Ophth* 28:525 (May) 1945.

instance, he did not state whether or not his patients had anomalous correspondence, he did not attempt to place the targets at the angle of anomaly (in which case no movement should occur if the theory is correct) His paper can thus be regarded only as a preliminary study, but it certainly opens up a new and extremely interesting method of investigating the normal and anomalous retinal relationship

The difficulties arising from the lack of familiarity with the older literature and from the confusion in the more recent literature on anomalous correspondence are clearly shown in a paper by Burri⁷³

Miss Burri examined the question as to what constitutes anomalous correspondence and concluded from the writings of Mayou, Pugh and Travers that the current opinion appeared to be that the objective and subjective angles have to coincide for the correspondence to be normal This, Burri stated, puts the theory of anomalous correspondence on anatomic or "anatomicoretinal" grounds, but none of the authors have given a "clear explanation of the anatomic function of abnormal correspondence" The theory of abnormal retinal correspondence has been developed from the basic hypothesis that exact retinal correspondence is an objectively demonstrable and invariable fact" and stands and falls with the validity of the basic hypothesis

Is, then, Miss Burri asks, normal correspondence, and consequently anomalous correspondence, an objectively demonstrable fact, or are they subjective inferences?

Her search of the neurologic literature remained inconclusive Some neurologic findings point toward a certain correspondence between retinal and cortical areas, yet considerable equipotentiality and mass action exist The study of the horopter is also unsatisfactory, since it is not "objective" but is based on "subjective inferential data"

In this paper, in the beginning of the section on the methods for the determination of anomalous correspondence, it was mentioned that there are ingenious laboratory methods for the determination of the distribution of the corresponding retinal points The determination of the empiric longitudinal horopter is one of them If Miss Burri had studied the work of Tschermak-Seysenegg,¹ she would have found ample information on the criteria of correspondence She would also have found that what she terms "subjective inferential data" are data of the highest accuracy and that the methods of the exact subjectivism² are in principle the only methods by which one can ever learn something about the subjective phenomena of correspondence and visual localization¹¹ Whether the anatomic and physiologic correlatives of these phenomena are a retino-cortical point to point relationship, or whether such factors as mass

⁷³ Burri, C The Concept of Abnormal Retinal Correspondence A Theoretical Analysis, Arch Ophth **19** 409 (March) 1938

action and equipotentiality are involved, is of great interest in itself but has no bearing on the theory of retinal correspondence

I believe that in the light of this knowledge she would probably have considered her own experimental evidence somewhat more critically. She studied three groups of patients: 40 without muscular imbalance, 40 with either esophoria or exophoria and 40 with esotropia or exotropia. All these subjects were tested on the synoptophore and were allowed to adjust the instrument so that the two pictures were superimposed. The figures thus obtained were compared with the figures resulting from the screen test, the parallax test and the perimeter test. Five or six trials were given each subject, and the largest and smallest deviations obtained with the synoptophore test and with the other tests were tabulated. The averages are given in a table for the three groups. The deviations are assumed to be a measure of the retinal correspondence.

Miss Burri found that none of the groups showed "exact retinal correspondence", the patients without muscular imbalance showed essentially the same deviation (maximum, about 3 degrees, minimum, 1 to 2 degrees), and the patients with strabismus, a somewhat larger deviation (maximum, 6 to 7 degrees, minimum, about 4 degrees).

It is quite apparent that this rough experiment can in no way influence the theory of retinal correspondence. Too many sources of error enter into the settings, such as size of image, fusional amplitudes, instrument convergence and single vision with Panum's areas, it is, however, surprising that all 40 patients with strabismus were able to superimpose macularly seen images and that there was no more than a deviation of 4 to 7 degrees from the objective angle. Without more information about such factors as the type of target and the selection of the strabismic cases, a real evaluation of the data is impossible. In any event, they do not justify the adoption of the empiristic theory of retinal correspondence, which Miss Burri again proposed.

In 1939 there appeared Chavasse's book on squint,²⁷ which is bound to have a profound influence on future thinking on the subject of strabismus. Written—even overwritten—in a refreshingly unorthodox style, dominated by one central idea, the book has the advantage of being an organic whole and has the earmarks of a work of art. New bottles are made, as Chavasse said, to hold the new wine of Sherrington, Magnus and Pavlov. Yet I believe that the book, so persuasively and brilliantly written, is dangerous to those who have not taken a long draft of the "old wine" of Helmholtz, Hering, Tschermak-Seysenegg, Javal and Bielschowsky.

All varieties of squint, Chavasse argued, appear as perversions or subversions of the normal binocular reflexes by various obstacles during and after the developmental period. Ontogeny, phylogeny, anatomy and

physiology are reviewed from this standpoint, and a new pathology of the binocular reflexes is evolved. In such a system, anomalous, or, as Chavasse called it, secondary, retinal correspondence naturally plays a large role. In fact, the concept of correspondence is extended, and even overextended, to a point where the whole concept becomes blurred, and the state of squint is defined as "a state of secondary correspondence." There is alleged to be a state of primary (or normal) motor correspondence, reflected in the correct position of the eyes, a primary (or normal) retinal correspondence, reflected in identical retinal projections, and a primary (or normal) proprioceptive correspondence between the two unocular proprioceptions, reflected in identical projections of the two foveovisual axes.

It is, of course, impossible to go into the wealth of detail of Chavasse's book, and I must restrict myself here to his statements relating to the theory of anomalous retinal correspondence.

Chavasse distinguished clearly between relative and egocentric spatial localization. According to him, the former is determined by the retinal correspondence, the latter by the proprioceptive correspondence. But he expressed the belief that "secondary retinal correspondence" can be properly appreciated only if "secondary proprioceptive correspondence" is added, the whole constituting a "perverted binocular fixation reflex."

It must be said, first of all, that "proprioceptive correspondence" is at best a dubious idea. It has been doubted, for good reason, that proprioception, particularly ocular proprioception, is a factor in spatial localization in man. Egocentric localization, on the other hand, about which little is known in concomitant strabismus, does not appear to be closely related to the behavior of retinal correspondence.

Chavasse's argument, though clothed in the language of reflexology, really resolves itself into the old projection theory, aided by the concept of the "muscle sense." And with it there remain all the difficulties of explaining the sensorial phenomena observed in concomitant strabismus. This is particularly evident in Chavasse's attempt at interpreting "monocular diplopia" and "binocular triplopia." To him, "the image of the erstwhile squinting eye is being projected in two directions, the normal retinal and the secondary proprioceptive." This most unsatisfactory explanation of a visual sensation by proprioception independent of a second visual sensation by retinoception was not clarified by Chavasse and, I believe, cannot be clarified.

Nor did Chavasse understand Hering's concept of corresponding retinal points. He stated that Hering stressed the anatomic correspondence heavily but that this anatomic correspondence is by no means exact. As proof, Chavasse cited the Kundt partition experiment and the deviation of the subjective from the objective vertical. Thus,

Chavasse, by substituting an assumption which was not made⁷⁴ (a mathematical distribution of corresponding points), used the very argument on which exact subjectivism is based and then concluded

allowance for the disparity is made, and can only be made, in virtue of a mechanism which is based upon proprioception of the state of version and vergence of the eyes, because the degree of disparity varies with this varying state

The degree of disparity does not vary with this varying state. The conclusion to be drawn from the disparity between objective and subjective space is that the position of the corresponding points can be determined only by subjective methods¹¹. It cannot be stressed too strongly that it is here that the clue to the understanding of anomalous correspondence lies.

To Chavasse, however, both normal and anomalous correspondence were conditioned reflexes. If the position of the eyes is such that the lines of gaze intersect in the fixation point, the proper habit in the use of the eyes will be established. This proper habit is the localization of the stimuli reaching the two foveas in identical subjective visual directions. If the lines of gaze do not intersect in the fixation point, the reflex is perverted. A common visual direction is established between the fovea of the fixating eye and an eccentric retinal element. With the passage of time, both the normal and the perverted conditioned reflexes become unconditioned, or automatic. From this theory Chavasse deduced his therapeutic principle: the early removal of motor or sensory obstacles which may produce the perversion or prevent the establishment of the normal binocular reflexes. Once the perverted binocular reflexes have become automatic, they cannot be normalized by any therapeutic procedure. Because of this, Chavasse was absolutely skeptical of orthoptic fusion training in any form.

To extend the concept of reflex to include, on the effector side, purely subjective phenomena may be accepted by the behaviorist school of thought. To me, the concept of reflex becomes devoid of meaning by this extension. Where there is no motor or secretory effect, there is no reflex, conditioned or otherwise. To include subjective phenomena in the objective sphere by making them the direct end result of reflex happenings makes the truly scientific investigation of either sphere impossible.

Chavasse's book must be read with discrimination. But it offers, in spite of its basic shortcomings, stimulating ideas about anomalous correspondence, its clinical significance and its determination.

⁷⁴ Hering stated explicitly: "Each visual direction is an imaginary mathematical line. But since vision is by no means mathematically exact, the visual directions may *in praxi* not be considered as mathematically exact. They are approximate determinations fluctuating within certain limits" (Hering,⁹ 1862, book 2, p. 159).

A paper by Hamburger⁷⁵ is apparently of importance in the theory of anomalous correspondence. Unfortunately, because of the prevailing conditions, I was unable to procure the original paper, which was published by *Albrecht von Graefe's Archiv für Ophthalmologie*, and I have only a short abstract of Hamburger's presentation before the Ophthalmological Society of Vienna. It seems from this abstract that in examination of patients with strabismus Hamburger combined the synoptophore method with an after-image method, thus permitting a direct check on the behavior of the visual directions. He concluded that changes both in the angle of squint and in the angle of anomaly may cause a change in the visual directions. But he also found that the change from normal to anomalous correspondence is gradual. When first degree pictures are presented, there is anomalous correspondence and the after-images are separated, with dissimilar patterns, owing to the compulsion to fusion, the eyes straighten and the after-images approach each other, forming a cross over the fused haploscopic image. Hamburger did not believe that normal and anomalous correspondence coexist, as was assumed by Bielschowsky in the explanation of cases with monocular diplopia. The movement of the after-images observed by Hamburger's patients could be explained on the basis of the ϕ phenomenon,⁷⁹ but until the details of his investigations are known it is not possible to evaluate his conclusions.

In 1942 Werner⁷⁶ attempted to demonstrate that the same principles can be shown to be effective in an abnormal retinal relationship and in normal binocular vision. He rejected what he claimed to be Hering's definition of corresponding points and introduced a "dynamic" concept of stereopsis, according to which binocular stereopsis is connected with a "functional change of projection," or functional displacement. The "change of projection," such as occurs in anomalous correspondence, was also thought to signify a functional displacement, and Werner further stated that analogous changes of correspondence occur in normal vision. It is impossible to present here fully the reasons that Werner's conclusions are fallacious, all that can be stated is that his premises are not sufficiently well founded to permit the far reaching conclusions which he has drawn and which deeply affect the theory of binocular vision. In another paper Werner's experiments will be dealt with in some detail.⁷⁷

75 Hamburger, F. A. Haploskopische Untersuchungen an Schielenden, *Klin Monatsbl f Augenh* **108**:235, 1942.

76 Werner, H. Binocular Vision Normal and Abnormal, *Arch Opth* **28** 834 (Nov) 1942.

77 Ogle, K. N., and Burian, H. M. The Stability of the Spatial Values of the Retina and the Theory of Stereopsis, to be published.

The most recent paper on anomalous correspondence is that by Swan ⁷⁸ He objected on three grounds to the definition of anomalous correspondence as a condition in which the fovea of one retina and an eccentric element of the other acquire a common visual direction, as given by Lancaster ⁶ He stated, first, that such a functional relation can be demonstrated in few patients with anomalous retinal correspondence This is contrary to fact In virtually every case it can be shown by the double image test that such a relationship does exist Secondly, Swan claimed that adoption of this definition is not expedient, because it may have misled ophthalmologists to believe that the condition is rare This statement he based on the fact that in a series of 100 consecutive patients with esotropia seen in the State University of Iowa Clinics in 1935, only 3 were suspected of having anomalous correspondence The test was performed with

an illuminated Brewster-Holmes type of prism stereoscope so adjusted that when one target was fixated by the fovea of the nonsquinting eye, the other target stimulated that peripheral retinal area of the squinting eye which, according to the aforementioned definition, could become a functionally corresponding point Correspondence was considered abnormal only if the two objects were superimposed

It is true, as Swan stated, that this test is fallacious—rather, that it has its limitations—but this does not substantiate Swan's claim that the definition is fallacious The definition does not state which retinal area of the squinting eye has common visual directions with the fovea of the fixating eye, i e, it is not restricted to cases of harmonious anomalous correspondence, as Swan seemed to imply in the foregoing citation, nor does it state that the patient will necessarily perceive simultaneously or fuse at the angle of anomaly ⁷⁹ Finally, Swan, in accordance with Harms, Travers and others, found that there is a region of suppression in the area of the retina of the squinting eye which supposedly has a common visual direction with the fovea of the fixating eye How, he asked, can the fovea of the fixating eye become a functionally corresponding point with a suppressed retinal area in the squinting eye? This situation has been discussed in a previous section of this paper It was stated that this typical interrelation between suppression and anomalous correspondence may well lead to an explanation of the origin of anomalous correspondence In any event, as was said before, the existence of such a relationship can always be demonstrated in the double image test

For the rest, Swan recognized that anomalous correspondence is a process of adaptation and that the findings may vary with the type

⁷⁸ Swan, K C Definition of Anomalous Retinal Correspondence, *Am J Ophth* 28 58, 1945

⁷⁹ Some writers, to be sure, say that the patient uses the macula of one eye with the nonmacular area of the other eye

of test used, and he advocated intensive orthoptic training immediately after operation to establish normal correspondence before an anomalous correspondence adapted to the new deviation develops

2 MONOCULAR DIPLOPIA AND BINOCULAR TRIPLOPIA

In 1924 Fischer⁸⁰ reported a case of binocular triplopia occurring after operation for convergent strabismus. The formerly deviated eye had a corrected visual acuity of 0.1. Fischer accepted Bielschowsky's⁸¹ explanation of the phenomenon for his own case and emphasized that it was a good example of the adaptability and elasticity of the sensorial apparatus.

Gredstedt⁸² also based the explanation of a case, which he briefly reported, on the coexistence of normal and anomalous retinal correspondence.

The whole subject of anomalous correspondence was well stated by Purdy⁸³ in connection with a case of monocular diplopia. This author studied in a psychologic laboratory an 18 year old student with strictly alternating convergent strabismus (visual acuity of 20/15 in each eye with a -1.25 D sphere for the right eye and 0.25 D sph $\subset +0.25$ D cyl, axis 7 for the left eye), who had been operated on at the ages of 5 and 14 years. There was a small residue of convergent strabismus and a hypertropia. The observer had permanent spontaneous diplopia, which he was able to disregard, the distance of the spontaneous double images corresponded to the angle of squint (normal correspondence). Under appropriate conditions, with either eye alone, there was monocular diplopia, the second image was to the right when seen with the left eye and to the left when seen with the right eye (indicating anomalous correspondence).

Purdy fully accepted the classic explanation of the phenomenon and stated the belief that his case furnished added support to the idea that the normal retinal correspondence is congenitally established but that it differs from others in that the monocular diplopia can be produced with either eye. Purdy assumed that the anisometropia in his case prevented the development of marked ocular dominance and hence made possible the acquisition of two anomalous systems.

It is not necessary to assume two anomalous systems to explain the case. The "anomalous system," the angle of anomaly, is the same no matter which eye fixates. Just as in any other case of convergent

80 Fischer, E. La neutralisation régionale dans un cas de triplopie binoculaire, postopératoire chez un strabique, *Ann d'ocul*, **161** 208, 1924.

81 Bielschowsky, A. Ueber monokulare Diplopie ohne physikalische Grundlage nebst Bemerkungen über das Sehen der Schielenden, *Arch f Ophth* **46** 143, 1898.

82 Gredstedt. Ueber einäugiges Doppeltsehen, *Ztschr f Augenh* **72** 243, 1930.

83 Purdy, D. M. Double Monocular Diplopia, *J Gen Psychol* **11** 311, 1934.

strabismus with anomalous correspondence, each fovea had acquired a common visual direction with an eccentric (nasal) element of the other retina. The distinctive feature of the case is that both the normal and the anomalous visual direction coexisted, producing monocular diplopia.

An interesting observation was reported by Purdy. When he attempted the experiment of color mixture with his subject, color mixture was never obtained, nor did the colors display rivalry or appear to be lying one behind the other. Instead, the two colors were seen simultaneously in the same place. Purdy concluded that there is a remarkable degree of independence between the binocular fields. The phenomenon is comparable to the one which I described,¹⁵ in which patients with permanent spontaneous diplopia saw "two objects in the same place" when one object, such as a pencil, was brought into the point of intersection of the patient's lines of gaze.

In their book on concomitant strabismus, Malbrán and Adrogué⁸⁴ reported 3 cases of binocular triplopia. Another case was reported by Adrogué and Lagos.⁸⁵ These authors were in agreement that the phenomenon is due to the persistence of the anomalous correspondence coexisting with the normal correspondence. They seemed to feel, however, that the monocular diplopia is not due to the localization in two visual directions of the foveal stimuli of the deviating eye, but rather, that it is the result of the visual direction of the eccentric element in the deviating eye which corresponds anomalously with the fovea of the fixating eye somehow coming into consciousness. Thus they stated that in binocular triplopia there are three images: one perceived by the fovea of the fixating eye, another perceived by the fovea of the deviating eye (in normal correspondence with the other fovea) and a third perceived by the region in the deviating eye which has a common visual direction with the fovea of the fixating eye. Since no stimulation of that area occurs in these cases (for instance, in the double image test), no "perception" can take place, and this interpretation is therefore without basis in fact. Sverdlück²⁶ expressed the opinion that the cases of Malbrán and Adrogué are not typical and convincing cases of monocular diplopia but gave no reason for his statement.

Cass⁸⁶ made an interesting contribution to the problem of monocular diplopia. She was able to produce the phenomenon on the synoptophore in a surprisingly large number of cases, namely, in 33 out of 70. In

84 Malbrán, J., and Adrogué, E. Estrabismo, Buenos Aires, El Ateneo, 1938, Sobre diplopia uniocular, Arch de oftal de Buenos Aires **13** 140, 1938.

85 Adrogué, E., and Lagos, E. J. J. A propósito de un caso de diplopia permanente postoperatoria (estrabismo), Arch de oftal de Buenos Aires **13** 512, 1938.

86 Cass, E. E. Monocular Diplopia Occurring in Cases of Squint, Brit J Ophth **25** 565 (Dec) 1941.

some of the cases (51.2 per cent) she could elicit it only by placing the arms of the synoptophore at the subjective angle, in others (15.2 per cent), only by placing the arms at the objective angle, and in a third group (33.3 per cent), by placing the arms at either angle. The synoptophore targets were fused in all these cases, but on flashing, a second image appeared in the uncrossed or the crossed position, according to whether the monocular diplopia was produced at the subjective or the objective angle. The average age at the onset of strabismus was lower in the group in which monocular diplopia could be elicited than in the group in which it could not. Patients with anomalous correspondence only, and some degree of binocular vision with it, usually had monocular diplopia but those whose binocular vision was rudimentary had no binocular diplopia. Patients with both normal and anomalous correspondence, when the normal correspondence was strong, usually had no monocular diplopia. In the majority of cases in which monocular diplopia could be elicited there was an equal degree of binocular vision whether the patient used the eccentric point or the macula of the deviated eye with the macula of the fixating eye.

In 1943 I published an observation⁴² which I consider to be related to binocular triplopia. In the case in question the patient, who had a facultative divergent strabismus, presented both normal and anomalous correspondence. On occasions, however, when the double image test was administered, the patient reported that he saw the two lights in a slightly uncrossed position (anomalous correspondence), yet at the same time he had the "mental impression" that the separation between the two lights was much greater and that the second image "should be" in a position corresponding to a crossed diplopia of 12 to 14 arc degrees (normal correspondence).

3 CLINICAL APPLICATION ANOMALOUS CORRESPONDENCE AND ORTHOPTIC TREATMENT

In 1927 Fischer⁸⁷ stated that orthoptic exercises can be successful only if there is normal retinal correspondence. Otherwise, exercises should be discontinued because of the danger of postoperative paradoxical diplopia. Fischer determined the state of the retinal correspondence with the amblyoscope and found an anomalous relationship in 50 per cent of the cases.

Braun,²⁴ for the same reason as Fischer, warned against the use of postoperative exercises in cases of deeply rooted anomalous correspondence. In an exhaustive study, carried out under the direction of Tschermak, he reported on a series of patients with convergent

⁸⁷ Fischer, E. Die Bedeutung der anomalen Korrespondenz der Netzhaut bei Übungen der Schielenden im Binokularsehen, *Russk oftal* 6 225, 1927, reviewed, *Klin Monatsbl f Augenh* 79 706, 1927.

strabismus, whom he divided into three groups. The first group (8 patients) had normal correspondence, the second (5 patients) showed both normal and anomalous correspondence, and the third (24 patients) had only anomalous correspondence. The prognosis as to the spontaneous restoration of binocular vision was good in the first group, doubtful in the second and very poor in the third.

The first to discuss anomalous correspondence in the American literature was Moncreiff.⁸⁸ He gave a short but excellent account of its essence, its methods of determination and the earlier literature, in a paper dealing also with other disturbances of the visual function in concomitant convergent strabismus. Moncreiff did not report any personal experiences, but he recognized the types of harmonious and unharmonious anomalous correspondence (the latter having developed out of the harmonious type by reduction in the angle of squint) described the areas of suppression found in the various groups and expressed agreement with the view that anomalous correspondence represents a sensorial adaptation to the squinting position of the eyes.

In 1934 Hine⁸⁹ stated that anomalous correspondence, determined with the synoptophore, exists in 70 per cent of squinters. He expressed the opinion that fusion training should not be given without regard to this, since otherwise the anomalous relationship may be encouraged. In the interest of restoration of binocular vision, Hine recommended operation prior to the age of 7 years.

In a paper on the possibilities of orthoptic training published also in 1934, Guibor⁹⁰ was not concerned with anomalous correspondence. His paper is mentioned here only because he called the angle of squint the "angle of anomaly," a terminology which is not recommended because of the confusion which such a use of the term would create.

Pugh⁹¹ reported that in dealing with 400 patients with strabismus she found anomalous correspondence in 169 (42 per cent) and normal correspondence in 226 (56 per cent). Of those with anomalous correspondence, 73 per cent had alternating squint and 27 per cent unilateral squint, of those with normal correspondence, 83 per cent had unilateral and 17 per cent alternating squint. Taking into account various sources of error, Pugh concluded that about 50 per cent of the squinters acquire anomalous correspondence.⁹²

88 Moncreiff, W. F. Disturbances of Visual Functions in Concomitant Convergent Squint, with Special Reference to Retinal Incongruity, *Arch. Ophth.* **2** 179 (Aug.) 1929.

89 Hine, M. L. The Orthoptic Treatment of Squint, *Brit. M. J.* **1** 329, 1934.

90 Guibor, G. P. Some Possibilities of Orthoptic Training, *Arch. Ophth.* **11** 433 (March) 1934.

91 Pugh, M. A. The Significance of False Projection in Squint, *Proc. Roy. Soc. Med.* **27** 1615, 1934.

It is of interest to note that Pugh mentioned vertical anomalous correspondence and that in some cases she even attributed ocular torticollis to it. She discussed, furthermore, the significance of anomalous correspondence with regard to the postoperative result and stated that a patient whose eyes were straightened while he had anomalous correspondence may do one of three things.

(a) He may, finding the visual axes parallel, develop a true projection and fuse with his eyes straight.

(b) He may pass through a transitional stage when he learns to readjust his projection so that he eventually adapts himself to the new position of the eyes. During this transition there is a false diplopia, in other words, a diplopia due not to faulty position of the eyes but to faulty projection of the visual images in space. He attempts to fuse the images with a false projection, and before the new projection is developed there is a tendency to recover some of the original deviation.

(c) He may show no sign of modifying his false projection, but retains it. Such a patient suffers from a troublesome false diplopia and in his efforts to overcome this symptom he reverts more or less to his original deviation.⁹¹

In a paper on the classification of concomitant strabismus, Pugh⁹³ spoke of anomalous correspondence only in connection with "fusion defect squints."⁹⁴ In the larger proportion of cases of strabismus of this type "false projection" develops. This gives the erroneous impression that anomalous correspondence occurs only in cases of this type. She further noted that the mechanism by which "false projection" is obtained appears to be chiefly cerebral, but that there is a specialized hypersensitive zone lying between the macula and the false projection spot. In a case of alternating squint, the spot on the retina of the deviated eye which corresponds in position to the macula of the fixing

92 It is of interest to compare these percentages with the old figures of F. Mugge (*Ueber anomale und normale Sehrichtungsgemeinschaft bei Strabismus convergens*, *Ztschr. f. Augenh.* **16** 110, 1906), who found that of his patients with anomalous correspondence 61.5 per cent had alternating squint and 27.4 per cent unilateral squint. P. A. Jaensch (*Die Dauererfolge der operativen Therapie des Ein- und Auswartsschielens*, *Klin. Monatsbl. f. Augenh.* **72** 86, 1924) found that 235 (83 per cent) of 283 patients with convergent strabismus and 53 (49 per cent) of 108 patients with divergent strabismus showed anomalous retinal correspondence. In the light of the old and more recent figures, Verhoeff's statement¹⁰ that it is commonly assumed that "anomalous projection" exists only in unusual cases is not understandable.

93 Pugh, M. A. *A Classification of Cases of Concomitant Strabismus Based on the Etiological Factor*, *Brit. J. Ophth.* **18** 466, 1934.

94 Among 500 cases Pugh found (1) squint due to refraction error in 62 per cent, (2) squint due to fusion defect in 15 per cent, (3) psychologic squint in 21 per cent and (4) squint due to physical defect in 2 per cent. The discussion preceding the figures in the paper is brief and incomplete, the classification appears artificial, and hence the figures are not meaningful.

eye appears to acquire a special localizing power in conjunction with the opposite macula. As to treatment, Pugh suggested that in a case of "fixed false projection" the best procedure is to try to develop "true projection" and fusion by training and then to operate. Training in a case of alternating squint with "fixed false projection" is tedious unless the treatment is aided by surgical intervention. She also warned that "false," or paradoxical, diplopia is a stubborn condition, not easily corrected by training. The patient she alleged, tries to fuse the images and, to do so, turns the eye back toward the original position of squint, and many of the disappointing results of operation are due to this state of binocular vision.

Chavasse,¹⁶ like Pugh, expressed the belief that the persistent absence of normal retinal correspondence, together with easily elicited anomalous correspondence, signifies that after operation there may be troublesome diplopia and paradoxical reflexes which tend to interfere to a greater or lesser degree, and for a longer or shorter period, with the result—even the merely cosmetic result—of operation. Chavasse was also pessimistic about the results of fusion training in cases of anomalous correspondence if the patient is over 6 years of age and if repeated tests by various methods fail to reveal any trace of normal correspondence. He considered these patients incurable by any form of treatment.

Goulden⁹⁵ stated that false projection may occur as an extremely serious complication of an operation for strabismus.

Miss Smith⁹⁶ also found that preoperative correction of an anomalous correspondence by orthoptic exercises is essential in insuring a good surgical result. She supported her contention by rather impressive statistical data. Of 30 patients who were operated on before normal correspondence was established, the eyes of only 4 remained straight in contrast to this, the eyes of 17 of the 19 patients in whom normal correspondence was established prior to the operation remained straight. On the other hand, of the 25 patients who had to begin with normal correspondence and were operated on, the eyes of 22 remained straight.

Statements about the deleterious influence of anomalous correspondence on the operative result are frequently heard,⁹⁶ and it is therefore worth while to stop for a moment to consider what they imply. They imply that after an operation for strabismus which has achieved parallelism or near-parallelism of the visual lines, the eyes may return more

95 Goulden, C. *The Principles of Orthoptic Training*, Tr. Ophth. Soc. U. Kingdom 55 576, 1935.

96 T. Keith Lyle,⁵⁴ for instance, spoke of "cases where a course of orthoptic treatment, in which binocular stimulation has been given at the subjective angle of squint, has been undertaken, with the result that after a carefully planned operation which has reduced the angle of deviation to 0°, the squinting eye has, in a few days after the pads have been removed, returned to its previously squinting position."

or less to their previous deviated position because of the persistent anomalous correspondence. This means that the motor conditions adapt themselves to the sensorial conditions, in other words, the old theory of Johannes von Müller, of incurable *strabismus incongruus*, is revived.

I do not believe that this pessimistic attitude is theoretically justified or practically borne out. In my experience with a very large number of cases of concomitant strabismus, I have never found anomalous correspondence a serious handicap to the obtaining of a good operative result. As compared with the large number of cases with anomalous correspondence treated by operation, the number of cases of troublesome postoperative spontaneous diplopia is negligible. The cosmetic result is just as good in cases with normal as in cases with anomalous correspondence. When the result was not satisfactory, I could almost always detect a mechanical reason for it. This applies to cases of normal as well as of anomalous correspondence.

In a paper published in 1935,⁹⁷ but not in a subsequent one published in 1941,⁹⁸ Feldman confused anomalous correspondence with aniseikonia. In the second paper he stated that he relied entirely on the synoptophore, since neither the congruence apparatus of Tschermak-Seysenegg nor the after-image test has proved satisfactory in the diagnosis and treatment of the conditions, because children are not always dependable in subjective tests. Feldman reported cures in about 50 per cent of his cases.

Penman⁹⁹ stated that in about 50 per cent of the cases of concomitant strabismus, mainly those in which the condition is of long duration and early onset and the angle is fairly large, anomalous correspondence is exhibited. In his opinion, treatment in cases of persistent anomalous retinal correspondence should be entirely cosmetic.

Much attention was given to anomalous correspondence by Malbran and Adlogué.⁸⁴ The physiologic basis of binocular vision was discussed at great length, and the sensorial behavior in cases of concomitant strabismus was studied in detail. The authors expressed the belief that the sensorial behavior offers the best criterion for a rational classification of the cases of strabismus. They found anomalous correspondence in 85 (or 55 per cent) of 153 cases of convergent strabismus, normal correspondence in 60 (39 per cent) and mixed correspondence (preoperatively) in 8 (5 per cent). Of the 26 cases of alternating convergent strabismus out of the total of 153, normal correspondence was present in only 4, anomalous correspondence in 20 and mixed

97 Feldman, J. B. Orthoptic Treatment of Concomitant Squint, *Arch. Ophth.* **13** 419 (March) 1935.

98 Feldman, J. B. Clinical Observations on the Treatment of Squint, *Arch. Ophth.* **26** 38 (July) 1941.

99 Penman, G. G. Treatment of Concomitant Squint by Orthoptic Methods. Some General Considerations, *Brit. M. J.* **2** 1019, 1937.

correspondence in 2. Thus the authors confirm the earlier statements that anomalous correspondence is particularly frequent among patients with alternating strabismus.

Cass,⁹¹ in 1938, gave a historical survey of the problem of anomalous retinal correspondence and reported percentages found by her on the basis of examinations with the synoptophore. Her figures (in condensed form) are reproduced in table 2.

Some interesting observations on anomalous correspondence were reported by Dicke.¹⁰⁰ This author considered both normal and anomalous correspondence to be a habit mechanism, the latter established as the result of simultaneous stimulation of noncorresponding points. For the diagnosis, Dicke used the after-image test, the diplopia test and a major synoptophore. She found that the anomalous correspondence was more firmly established if it was evident in all three tests. In some

TABLE 2—*Results of Examination on the Synoptophore in 500 Cases of Strabismus*

	Convergent Strabismus 383 Cases (77.6%)		Divergent Strabismus 107 Cases (21.4%) All Types	Vertical Strabismus 5 Cases (1%) ++
	Unilateral 38 Cases	Bilateral 50 Cases		
Anomalous correspondence only	20.1%	54%	12%	
Normal and anomalous correspondence	22.2%	8%	8%	60%
Normal correspondence	49.1%	72%	67%	20%
Suppression	8.6%	6%		20%

cases the anomalous correspondence quickly yielded to normal correspondence by macular stimulation, sometimes after twenty to thirty minutes of this procedure even the after-image test showed a normal retinal relationship. Dicke looked on the prognosis in these cases as being favorable. As to the length of the treatment (constant occlusion and regular periods of orthoptic exercises several times a week), Dicke expressed the belief that failure to improve after four or five months constitutes a fair trial.

The preoperative and postoperative treatment of anomalous correspondence was also outlined by Mann.⁹⁶ She, too, emphasized the value of occlusion and stressed particularly the importance of directing the patient's attention properly during the exercises.

VII TERMINOLOGICAL COMMENTS

It is apparent from many of the more recent papers in which anomalous correspondence is discussed that much of the misunderstanding and confusion is due to a lack of clarity in the terminology.

¹⁰⁰ Dicke, D. E. Anomalous Retinal Correspondence. *Am J Ophth* 25:585, 1942.

It seems desirable, therefore, to conclude this paper with a few comments on terminology

The oldest term used to designate an anomalous retinal relationship is "retinal incongruity" (incongruous retinas, strabismus incongruus). Introduced, I believe, by Johannes von Muller and used by von Graefe, it occurs occasionally in the recent literature (Moncreiff,⁸⁸ Feldman,⁹⁷ and others). This term should not be used. It is equivocal and gives rise to confusion, since it is properly used to designate physiologic and pathologic discrepancies existing in normal correspondence (which is why Feldman confused aniseikonia and anomalous correspondence).

Another term which is occasionally encountered is "false associated fixation" (Alabaster,¹⁰² Lyle and Jackson¹⁰³). This term is not well chosen. The association is not false, the fixation relates only to one eye, but the thought which probably prompted the coming of the term may be correct.

I come now to the large group of terms which center around "projection" and "correspondence." The expressions "false and true projection" are widespread in the orthoptic literature, although some authors (Lyle and Jackson¹⁰³, Smith,³⁵ and others) recognized that it may give rise to confusion "with the malprojection of one eye, present in paralytic squint" (Lyle and Jackson¹⁰³). There are, however, stronger reasons that these expressions, and the analogous terms "normal and anomalous projections," should be relinquished. Not only do they lead to a confusion of absolute and relative spatial localization, but they embody a fallacious theory, the projection theory of spatial localization.

The terms "true" and "false" are also subject to criticism. I do not believe it to be good usage to speak of true and false images,¹⁰⁴ true and false angles, true and false projection, true and false correspondence. Because a phenomenon is subjective, it does not follow that it is false. There is nothing "false"—phenomenologically or otherwise—about a second image or any mode of localization in subjective space. Such second images, or a particular mode of localization, may be normal or anomalous, according to whether they follow the law of normal common visual directions. Spatial localization may be "correct" or "incorrect" (according to whether the phenomenal or the subjective appearance is in accordance with the objective localization of the stim-

101 Footnote deleted

102 Alabaster, E. B. Remarks on the Physiology of Convergent Concomitant Strabismus, *Tr. Ophth. Soc. U. Kingdom* 55: 321, 1935.

103 Lyle, K., and Jackson, S. Practical Orthoptics in the Treatment of Strabismus, ed. 2, Philadelphia, The Blakiston Company, 1941.

104 It is regrettable that there is no English equivalent for the German term *Halbbild*.

ulating object points), but there is never anything "false" about it¹⁰⁵ I believe, therefore, that the expressions "true" and "false" should be altogether abandoned and replaced by "normal" and "anomalous" In speaking of angles or spatial localization, "subjective angle" and "objective angle," or "subjective localization" and "objective position," should be used

The term "anomalous correspondence" is probably more frequently employed now than any other term to denote an anomalous sensorial retinal relationship in strabismus But this term, too, has its weakness, as was first pointed out by Tschermak-Seysenegg³⁰ and more recently, on similar grounds, by Verhoeff¹⁰ Tschermak-Seysenegg pointed out that the normal retinal relationship—the "normal retinal correspondence"—rests on an innate basis, is elementary and fixed and is connected with the system of horizontal disparity by which binocular depth perception or stereopsis is achieved The "anomalous retinal correspondence," on the other hand, connects retinal elements of very different visual acuity, it varies under the influence of both exogenous and endogenous factors (i e., it is not fixed, but unstable), depth perception does not come about through horizontal disparities on the basis of an anomalous retinal relationship, although rudimentary fusional movements may be elicited on that basis

Consequently, Tschermak-Seysenegg reserved the expression "retinal correspondence" for the normal sensorial retinal relationship and coined the German term *anomale Sehrichtungsgemeinschaft* to indicate the one main characteristic of any anomalous sensorial retinal relationship, namely, that *de norma* disparate retinal elements have acquired, as an anomaly, a common visual direction Tschermak-Seysenegg, therefore, did not accept terms such as pseudocorrespondence, pseudofovea or secondary correspondence (von Kries, Chavasse) Similar considerations apply to such expressions as "maculo-macular correspondence" (Chavasse) or, simply, "macular correspondence" (Cass⁶¹) or "maculo-pseudomacular correspondence"

There is no English equivalent for Tschermak-Seysenegg's *anomale Sehrichtungsgemeinschaft* Attempts to translate it directly result in clumsy terms which are not appropriate for routine use I have tried to evade this difficulty by adopting in the present paper the expression "normal and anomalous sensorial retinal relationship" This is a neutral expression which does not imply any theory and merely states a fact It is, however, rather unwieldy, and I doubt, therefore, whether it will become generally accepted I believe that, on the whole, the expression

105 It is, accordingly, normal for a person who places a meridional size lens at axis 90 in front of one eye to perceive under certain conditions a distortion of his subjective space—it would be anomalous if he did not—but he now localizes objects incorrectly

"anomalous (retinal) correspondence," best satisfies the clinical needs and should be used, provided that the essential differences between "normal and anomalous correspondence" are kept in mind

The terms "objective" and "subjective angle" have already been mentioned. The difference between the two represents the "angle of anomaly," or "angle of adaptation", the former expression, being purely descriptive, is probably preferable. The term "quotient of perversion" (Chavasse) also implies a theoretic assumption (that both normal and anomalous correspondence are "reflexes") and is, therefore, not recommended.

The expressions "harmonious" and "unharmonious," or "subharmonious," anomalous retinal correspondence are convenient to indicate whether or not the angle of anomaly is equal to the angle of squint. The expressions "total" and "partial" anomalous correspondence used by Grant¹⁰⁶ in this sense are meaningless and should not be adopted.

VIII CONCLUSIONS

An anomalous sensorial retinal relationship is found in a large number of cases of concomitant strabismus. It represents an adaptation of the sensorial apparatus of the eyes to their abnormal relative position. Its essence consists in the acquisition of more or less stable common visual directions between *de norma* disparate retinal elements. It is not a condition in which common visual directions are absent, as has been claimed.

This anomalous sensorial retinal relationship cannot be understood, nor can all the accompanying phenomena be explained, on the basis of the projection theory of spatial localization. Only the theory of the subjective visual directions, on the broad foundation of the methods of exact subjectivism, permits a satisfactory understanding of all pertinent phenomena. It must also be clearly recognized that the anomalous retinal relationship refers to the relative spatial localization. It must not be confused with anomalies in the absolute (egocentric) localization, such as occur in cases of recent paralyses of the ocular muscles.

Clinical observations on the group of patients with mixed correspondence in whom strabismus has existed since the earliest days of life clearly show that normal retinal correspondence is the result of an innate preformed mechanism.

Anomalous correspondence, on the other hand, is acquired through usage. It is closely connected with other sensorial phenomena in concomitant strabismus, such as regional inhibition. A number of conditions are required for its establishment, time, usage and individual adaptability are most important. The basic factor in the stability of the

¹⁰⁶ Grant, H. W. Some Observations on Divergent Strabismus with Anomalous Retinal Correspondence, *Am J Ophth* 28 472, 1945

anomalous correspondence is the stability of the relative position of the eyes. The more stable the latter, the more stable is the anomalous sensorial retinal relationship.

The results obtained in the various types of tests devised for the determination of the sensorial retinal relationship in patients are a measure of this stability. The more deeply the anomalous correspondence is rooted, the more consistently will it be found to be present under all the different test conditions.

The therapy of anomalous correspondence, so essential for the functional cure of strabismus, presents a most difficult problem. Only a full grasp of the essence of the condition can make an evaluation of past achievements possible and insure progress in the future.

520 Commonwealth Avenue

Clinical Notes

METHOD FOR THE MAINTENANCE OF STERILITY OF OPHTHALMIC SOLUTIONS

Gilbert N Haffly, MD, and Carl D F Jensen, MD, Seattle

It is well known that the majority of ophthalmic surgeons are suspicious of the sterility of the ophthalmic solutions presented for use during the course of a surgical procedure on the eye and in the postoperative care. This skeptical attitude extends from the confines of the smallest community or private hospital to the marble halls of the greatest teaching institutions. It manifests itself by the dubious regard with which ophthalmic surgeons and surgical nurses view the varied assortment of dropper bottles present on the average eye-dressing tray. Praiseworthy attempts are regularly made to assure the sterility of such ophthalmic solutions by ordering frequent resterilization of those solutions commonly used in the surgical and postoperative surgical care of ophthalmic patients, particularly those who have undergone intraocular operations. However, from the moment a sterilized dropper bottle is opened its contents cease to be sterile.

Post¹ has pointed out that despite the fact that in recent years ophthalmic surgeons have conformed more closely to the concepts of asepsis existent in general surgery, such as the wearing of rubber gloves, the incidence of infection in ophthalmic surgery remains only slightly altered. He advanced the plea that ophthalmologists should search in every direction for any additional precaution that may prevent the tragedy of the postoperative infection.

Despite the well known fact that by no possible method can the conjunctiva be rendered completely sterile, no ophthalmic surgeon would care to feel guilty of introducing pathogenic organisms into the eye which has been operated on. The need for a simple and convenient method of maintaining the sterility of ophthalmic solutions is apparent.

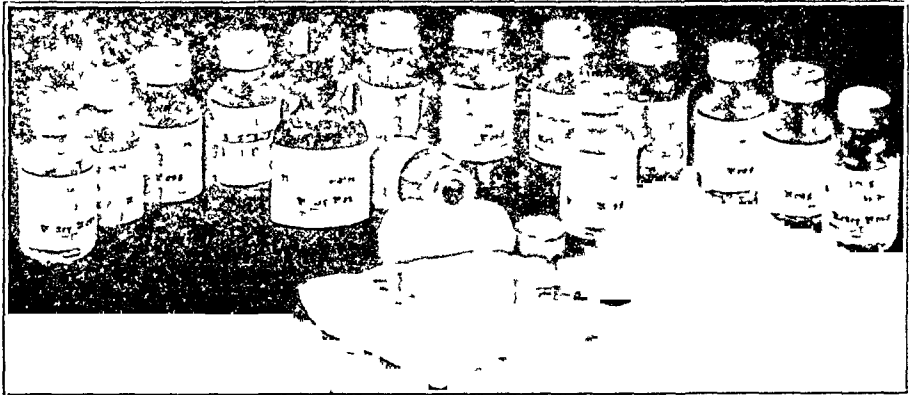
The picture presented is self explanatory. A sterilized cotton applicator is utilized to paint the rubber cork of the stoppered vial with tincture of zephiran chloride. The detergent and germicidal effects of this powerful drug are sufficient to render the corked surface of the vial sterile in a matter of several seconds. Since the picture exhibited was taken, a change of importance has been suggested. To prevent the possible careless introduction of zephiran chloride into the eye, however unlikely, the bottle of tincture of zephiran chloride should not be of the drop bottle type, but, rather, should be one with a simple screw-on cap. The sterile 2 cc syringe and needle is utilized to withdraw the sterile contents of the solution desired. It has been found that by expressing the contents of the syringe through the tip of the hypodermic needle

¹ Post, M H, Jr. Dust-Borne Infection in Ophthalmic Surgery, *Tr Am Ophth Soc* 43 79, 1945

the controlled formation of individual drops is assured. The vials may be resterilized at desired intervals. Since labels are frequently lost during the course of sterilization, the vials must be permanently marked appropriately to prevent any possible confusion as to the contents of each and every vial. A special heat-resistant ink is used for this purpose.

PHARMACOLOGIC PROCEDURE

The material is dissolved when indicated in acid buffer solution (boric acid, 12.4 Gm., potassium chloride, 7.4 Gm., distilled water, q. s. 1,000 cc.) and adjusted with alkaline buffer solution (sodium carbonate anhydrous, 21.2 Gm., distilled water, q. s. 1,000 cc.) to the desired p_H according to Gifford's scale. Twenty cubic centimeter, rubber-capped vaccine vials, after thorough cleansing, are washed out with successive rinsings of filtered distilled water. The solution is then filtered into the vial through the same funnel and filter paper used in



Method of maintaining sterility of ophthalmic solutions

the rinsings. This provides a well washed filter paper and eliminates all particles of paper or dust. The vial is then capped and autoclaved at 240 F. for twenty minutes.

NOTE—A suitable eye-dressing tray of stainless steel that can be put in the autoclave with the vials in place is being made and will be the subject of a future article.

1315 Medical Dental Building (1)

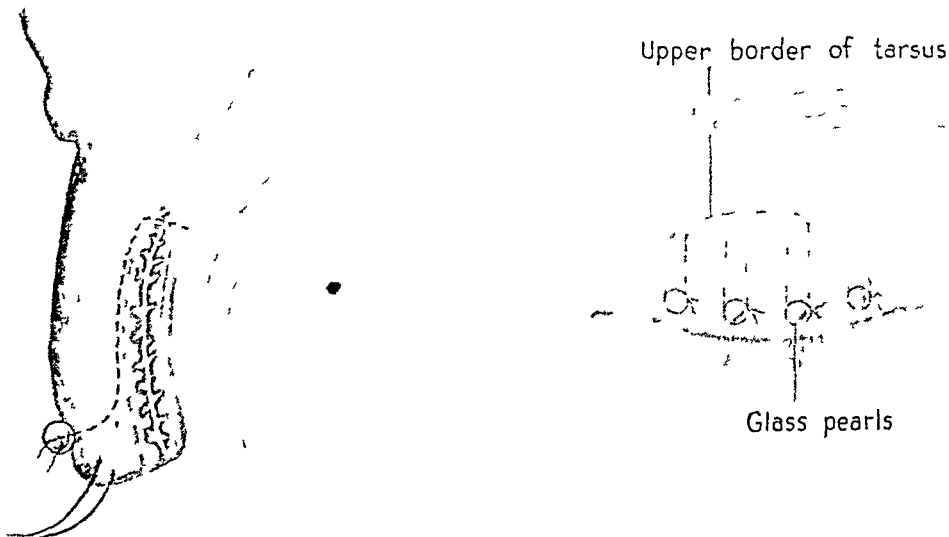
A SIMPLE MODIFICATION OF OPERATIONS FOR ENTROPION OF THE EYELIDS

RUDOLF H. BOCK, M.D., PEIPING, CHINA

Working in a country where trachoma is responsible for about one half of all the ophthalmic cases and where, therefore, operative procedures to correct entropion and trichiasis make up 30 to 40 per cent of all the operations, one tries to find simpler methods to substitute

for the complicated and time-consuming plastic procedures, such as the Hotz and Snellen operations

The method described makes use of the principle of the Hotz operation, *i. e.*, to fix the margin of the lid to the upper border of the tarsus by sutures. This, however, is done without cutting the skin, but only by passing three or four double-armed sutures from the conjunctival side through the upper border of the tarsus, then along the anterior surface of the tarsus downward and finally emerging through the skin 1 to 2 mm above the row of eyelashes. The other end of the silk suture is passed in the same way about 2 mm away from the first one, and the two are tied on the skin side over a glass pearl on a small gauze roll after exerting the necessary pull to produce the desired correction. There should be some overcorrection immediately after operation, as the sutures will always cut a little into the tissue later on. It is impor-



Modification of the Hotz operation for entropion of the eyelid

tant that all the three or four pairs of sutures come out at exactly the same level. An intermarginal incision may or may not be performed. The stitches are left in position for eight to ten days. Special care should be taken on changing the dressing to avoid stitch infection.

The advantage of this procedure is its simplicity and the fact that it causes very little trauma. It will be indicated mainly in cases of relatively mild entropion, in which the tarsus is not much thickened or curved by scar tissue. Cases of severe entropion remain the domain of major operations which also correct the shape and position of the tarsus. Entropion of the lower lid can be corrected by the same method, but the effect will be not so great because of the narrowness of the tarsus of this lid. In cases with acute inflammation of the conjunctiva this method should not be used for fear of stitch infection from the conjunctival side. A spastic entropion may be operated on with good results by this method, which can be indicated as a cosmetic procedure only.

INSTRUMENTS FOR USE IN OPHTHALMIC SURGICAL PROCEDURES

Carl Apple, M D, Chicago

CORNEAL SCISSORS

This instrument is a modification of the Walker scissors. The lower tip extends 1 mm beyond the upper tip, the extended part is 1 mm wide, the extreme end is rounded, and the surface is highly polished. This enables the operator to enter the anterior chamber with less difficulty and without trauma to the iris after the original section

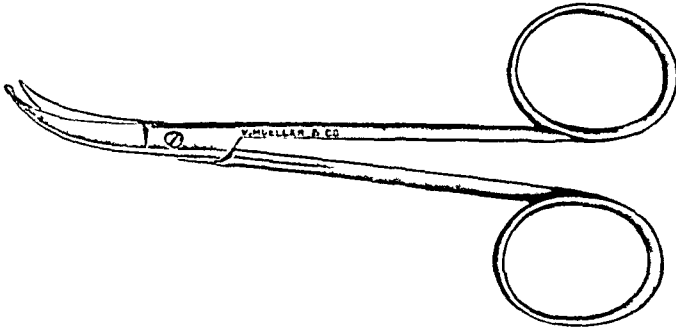


Fig 1—Corneal scissors

of the cornea with a keratome, or whenever the corneal section has to be enlarged. This scissors should also be useful in removing strips of sclera in eye-shortening operations. I have used the scissors for several years and have found them very useful. Precaution must be taken to have them very sharp at all times.

IRIS REDEPOSITOR

My associates and I have used this iris redepositor at the Research Hospital of the University of Illinois for the past six years and have found it a valuable instrument. The handle may be rounded or square,



Fig 2—Iris redepositor

the round handle enables the operator to rotate it between the thumb and the index finger. The redepositor portion is bent at an angle of 115 degrees and is 5 mm long and 2 mm wide, the extreme end is rounded and dull, and the surface is highly polished.

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Ophthalmologic Reviews

HYPOVITAMINOSIS A IN OPHTHALMOLOGY

R L SCHMIDTKE, M D

ST PAUL

INTRODUCTION

Purpose—The signs and symptoms of gross vitamin A deficiency both in experimental animals and in human subjects are well known to all students of medicine and nutrition and will not be discussed in this paper. A satisfactory presentation of the accepted clinical manifestations of vitamin A deficiencies may be found in Duke-Elder's "Text-Book of Ophthalmology." In reviewing the literature with reference to vitamin A deficiency, it has been my aim to correlate the thoughts and experiences of the various authors, so that a better clinical application of the known facts may be made.

Nomenclature—The term "hypovitaminosis" has been chosen because the word "avitaminosis" carries a meaning of complete absence of the vitamin under consideration. Such a condition is difficult to attain experimentally if the animal is provided with an adequate diet except for the vitamin under observation and probably never exists so far as the human case of vitamin deficiency is concerned.

Vitamins in General—Vitamins, important as they are for the maintenance of health and well-being, have been taken over by the makers of "patent remedies" and are being sold to the general public under a variety of attention-compelling names and without the physician's advice or prescription. Vitamins lend themselves well to this type of exploitation of the public because their toxicity is low and their importance to general health cannot be denied. It is for this reason, I believe, that conservative medical men try to avoid the diagnosis of "hypovitaminosis" as often as possible, especially in this country, because Americans as a group are better fed than any other people in the world. Nevertheless, I feel that Duke-Elder¹ presented the case of vitamin deficiency well when he stated

Thesis submitted to the Graduate Faculty of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Ophthalmology, June 1946

¹ Duke-Elder, W S. Text-Book of Ophthalmology, St Louis, C V Mosby Company, 1938, vol 2, p 1424

Although the deficiency diseases are dramatic and interest-compelling clinical entities, it is probable that the greatest importance of vitamin deficiency in clinical medicine lies in borderline cases of ill health which frequently puzzle the physician and disable the patient. It is quite possible that in partial avitaminosis the cumulative damage to the important epithelial structures of the eye—the cornea, the lens, and the retina—may lower their vitality, favor the incidence and prolong the activity of infections and precipitate degenerative changes on a wider scale than is yet realized. Nor should their therapeutic application be limited to the treatment of frank evidences of deficiency.

Vitamin A—Sometimes referred to as the ophthalmic vitamin, vitamin A was the first of these important dietary factors to be discovered by McCollum and Davis.² That xerophthalmia, keratomalacia and night blindness are the ocular signs and symptoms of hypovitaminosis A has been established by numerous animal experiments, foremost of which are the work of Mori,¹ Yudkin,³ Gudjonsson⁴ and Johnson⁵, the studies of Blegvad⁶ and his conclusion that xerophthalmia, keratomalacia and xerosis conjunctiva in Denmark during the period 1909 to 1920 was a vitamin A deficiency, the extensive observations of Pillat⁷ on effects of vitamin A deficiency in China, and the studies on

2 Jackson, E. The Ophthalmic Vitamin, editorial, *Am J Ophth* **18** 967, 1935. Duke-Elder,¹ p 1423.

3 McCollum, E. V., and Davis, M. Observations on the Isolation of the Substance in Butter Which Exerts a Stimulating Influence on Growth, *J Biol Chem* **19** 245, 1914.

4 Mori, S. Primary Changes in Eyes of Rats Which Result from Deficiency of Fat-Soluble A in Diet, *J A M A* **79** 197 (July 15) 1922.

5 Yudkin, A. M. (a) Ocular Manifestations of Rats Which Result from Deficiency of Vitamin A in Diet, *J A M A* **79** 2206 (Dec 30) 1922, (b) Ocular Disturbances Produced in Experimental Animals by Dietary Changes. Clinical Implications, *ibid* **101** 921 (Sept 16) 1933, (c) Clinical Implications of Ocular Disturbances Produced in Experimental Animals by Dietary Changes, *Tr Sect Ophth, A M A*, 1933, p 27, *Arch Ophth* **11** 902 (May) 1934. (d) Yudkin, A. M., Orten, M. S., and Smith, A. H. The Production and Cure of Ocular Disturbances in Adult Albino Rats by Adjustment of Vitamin A. Clinical Implications, *Am J Ophth* **20** 1115, 1937.

6 Gudjonsson, S. V. Xerophthalmia in Rats and Periocular Reaction, *Acta ophth* **8** 184, 1930.

7 Johnson, M. L. Degeneration and Repair of the Rat Retina in Avitaminosis A, *Arch Ophth* **29** 793 (May) 1943.

8 Blegvad, O. Xerophthalmia, Keratomalacia, and Xerosis Conjunctivae, *Am J Ophth* **7** 89, 1924.

9 Pillat, A. (a) Frequency of Deficiency Diseases of the Eye Due to Lack of Vitamin A in a Military Camp North of Peiping, *Nat M J China* **15** 585, 1929, (b) Main Symptoms of the Eye in Vitamin A Deficiency in Adults, *ibid* **15** 614, 1929, (c) Prexerosis and Xerosis of the Cornea as Independent Disease. Pictures of Eye in Deficiency Disturbances of Adults, *Arch f Ophth* **124** 486, 1930, (d) The Classical Symptom Complex of Vitamin A Deficiency, *Wien klin. Wchnschr* **53** 779, 1940.

experimentally induced vitamin A deficiency in human volunteers by Mandelbaum and Hecht,¹⁰ Steffen, Bair and Sheard¹¹ and others Vail,¹² in his editorial on vitamin therapy in ophthalmology, stated

It is but natural that in the enthusiastic reception of this knowledge, abuses should have crept in. If the history of any drug or healing agent be investigated, this same abuse at the onset of its application will be found. A search of the medical literature of the past will disclose serious articles in first-rate journals by outstanding men, devoted to astonishing reports of successful therapeutic results, in all sorts of conditions.

Patients with ocular diseases, the treatment of which has baffled the ophthalmologist in the past, are now being enthusiastically dosed with one or more of the vitamins, sometimes without any apparent logic. Vitamin A has been prescribed and reported on in the treatment of such varying conditions as tuberculous diseases of the eye,¹³ phlyctenular conjunctivitis,¹⁴ follicular conjunctivitis,¹⁵ keratoconjunctivitis sicca,¹⁶ keratitis superficialis,¹⁷ asthenopia,¹⁸ myopia¹⁹ and trachoma,²⁰ while

10 Mandelbaum, J, and Hecht, S. Dark Adaptation Under Controlled Dietary Vitamin A Conditions, *Am J Physiol* **129** 416, 1940, Dark Adaptation and Experimental Human Vitamin A Deficiency, *ibid* **130** 651, 1940

11 Steffen, L F, Bair, H L, and Sheard, C. Dark Adaptation and Dietary Deficiency in Vitamin A, *Am J Ophth* **23** 1325, 1940

12 Vail, D. Vitamin Therapy in Ophthalmology, editorial, *Am J Ophth* **24** 1325, 1941

13 Sal Lence. Vitamin Therapy in Ophthalmology, *Arch de oftal hispano-am* **31** 386, 1931. Frommopoulos, J. What Influence Has Vitamin A Deficiency on the Development of the Relapsing Seasonal Disease, Allergic (Scrofulous) Keratoconjunctivitis? *Klin Monatsbl f Augenh* **104** 1, 1940, A and C Hypovitaminosis in Case of Tuberculous Disease of the Eye, *ibid* **105** 707, 1940

14 Tai M C. Hypodermic Injections of Carotene in Treatment of Phlyctenular Conditions and Vitamin A Deficiency Diseases in Ophthalmology, *Chinese M J* **50** 1453, 1936

15 Sandels, M R, Cate, H D, and Wilkinson, K P. Follicular Conjunctivitis in School Children's Expression of Vitamin A Deficiency, *Am J Dis Child* **62** 101 (July) 1941

16 (a) Grósz, S. Etiology and Treatment of Keratoconjunctivitis Sicca, *Klin Monatsbl f Augenh* **97** 472, 1936. (b) Gifford, S R. Vitamin Therapy in Ocular Conditions, *Arch Ophth* **30** 162 (July) 1943. (c) Gifford, S R, Puntenney, I, and Bellows, J. Keratoconjunctivitis Sicca, *ibid* **30** 207 (Aug) 1943

17 Stocker, F. Keratitis Superficialis and Vitamin A, *Schweiz med Wchnschr* **66** 335, 1936

18 Cordes, F C, and Harrington, D O. Asthenopia Due to Vitamin A Deficiency, *Am J Ophth* **22** 1343, 1939. Newton, F H, and Schade, A H. An Experiment to Determine the Conservation of Vitamin A in the Eye Under Strain, *Ohio State M J* **39** 827, 1939. Pett, L B. Riboflavin and Vitamin A in Relation to "Eyestrain," *Canad M A J* **49** 293, 1943

Levine²¹ and Casini²² expressed the belief that a vitamin A deficiency may be the underlying cause of retinitis pigmentosa and Dor²³ stated the opinion that insufficiency of vitamin A might be a factor in the development of strabismus when there is a hereditary predisposition. Keratoconus has been experimentally produced in rats by Mutch and Richards,²⁴ while Hale²⁵ produced anophthalmos, in pigs and Warkany and Schraffenberger²⁶ induced congenital malformations in rats through vitamin A deficiency in the mothers. From the foregoing evidence, it is obvious that there are "tares among the wheat." Again, quoting from Vail's¹² editorial:

The only way in which our prejudices can be debunked is by the publication of articles by competent and trustworthy observers who have access to a large amount of clinical and experimental facilities. The question, "Is this honest work?" must be constantly posed. Subtle influences such as the desire to satisfy enthusiastic ambition, or to promote the interests of pharmaceutical benefactors must be searched for and weighed in the balance by the reader. The logic of the drug action must be apparent to some extent at any rate. Finally, the test of one's own experience must be made and impressions turned into facts by observation.

NIGHT BLINDNESS AND DARK ADAPTATION

Nomenclature—According to Dorland,²⁷ the term "nyctalopia" is derived from the Greek words meaning "night-blind eye," while the term "hemeralopia" is derived from the Greek words meaning "day-blind eye." Since each term has been used in the literature to mean both night and day blindness, the term "night blindness" will be used in this paper to avoid confusion. Many of the authors cited here, however, have used the word "hemeralopia" to designate "night blindness."

Vitamin A and Night Blindness—That a lack of vitamin A in the diet will cause functional night blindness has been definitely established by

19 Laval, J. Relationship Between Myopia and Avitaminosis, *Am J Ophth* **24** 408, 1941. Guha, G. S. The Role of Vitamins in Ocular Affections, *Proc All-India Ophth Soc* **4** 82, 1935.

20 Kendall, A. I., and Gifford, S. R. Trachoma and Avitaminosis, *Arch Ophth* **4** 322 (Sept.) 1930.

21 Levine, J. Is Retinitis Pigmentosa Due to Vitamin Deficiency? *Arch Ophth* **9** 453 (March) 1933.

22 Casini, F. Retinitis Pigmentosa and Avitaminosis, *Arch di ottal* **42** 409, 1935.

23 Dor, L. Strabismus and Avitaminosis, *Arch d'opht* **50** 667, 1933.

24 Mutch, J. R., and Richards, M. B. Keratoconus Experimentally Produced in Rat by Vitamin A Deficiency, *Brit J Ophth* **23** 381, 1939.

25 Hale, F. The Relation of Vitamin A to Anophthalmos in Pigs, *Am J Ophth* **18** 1087, 1935.

26 Warkany, J., and Schraffenberger, E. Congenital Malformations Induced in Rats by Maternal Vitamin A Deficiency, *Arch Ophth* **35** 150 (Feb.) 1946.

27 Dorland, W. A. The American Illustrated Medical Dictionary, Philadelphia, W. B. Saunders Company, 1938.

the studies, observations and experiments of such men as Fridericia and Holm,²⁸ Holm,²⁹ Yudkin,^{5c} Pillat^{9a,b,d} and Aykroyd,³⁰ and Eusterman and Wilbur³¹ quoted Hippocrates as advocating the use of an abundance of liver and honey in cases of night blindness. However, as has been pointed out by Feldman³² and Manville,³³ not all cases of night blindness are due to vitamin A deficiency. Certain organic diseases, such as glaucoma, choroiditis, optic neuritis, retinitis pigmentosa and retinal detachment, have some degree of night blindness as one of the symptoms, but, as pointed out in Post's³⁴ editorial on vitamin A deficiency, it would not be illogical to assume that in these diseases in which night blindness is an important symptom a vitamin A deficiency might be suspected as an etiologic factor. The night blindness associated with the aforementioned ocular diseases has been referred to only in order more nearly to complete the picture. It is my opinion, based on my review of the literature, that few, if any, of these conditions have vitamin A deficiency as an underlying cause.

Night Blindness and Dark Adaptation—Most investigators seem to take for granted that night blindness and poor dark adaptation are synonymous. Yudkin³⁵ warned that "It is important to decide whether hemeralopia and poor dark adaptation are synonymous, for at present investigators are classifying poor dark adaptation as hemeralopia, and some have gone still further and assumed that poor dark adaptation or hemeralopia is a sign of vitamin A deficiency. I cannot fully subscribe to the latter assumption until further investigation is made," while Woisika³⁶ stated that "In the present state of knowledge of scotopic vision, the term 'night blindness' and 'poor dark adaptation' should not be used synonymously as to tests."

28 Fridericia, L. S., and Holm, E. Experimental Contributions to the Study of the Relation Between Night Blindness and Malnutrition, *Am J Physiol* **73** 63, 1925

29 Holm, E. Demonstration of Hemeralopia in Rats Nourished on Food Devoid of Fat-Soluble A Vitamin, *Am J Physiol* **73** 79, 1925

30 Aykroyd, W. R. Night Blindness Due to Vitamin Deficiency, *Tr Ophth Soc U Kingdom* **50** 230, 1930

31 Eusterman, G. B., and Wilbur, D. R. Clinical Features of Vitamin A Deficiency, *J A M A* **98** 2054 (June 11) 1932

32 Feldman, J. B. Dark Adaptation, Night Blindness, and Glaucoma, *Arch Ophth* **22** 595 (Oct) 1939

33 Manville, I. A. Nutrition and Night Blindness, *Northwest Med* **38** 208, 1939

34 Post, L. T. Vitamin A Deficiency, editorial, *Am J Ophth* **19** 617, 1936

35 Yudkin, A. M. Vitamins in Treatment and Prevention of Ocular Diseases, *Arch Ophth* **19** 366 (March) 1938

36 Woisika, P. H. An Evaluation of the Dark Test, *Ann Int Med* **21** 101 1944

Dark Adaptation —Dark adaptation is the ability of the eye to adjust from illumination of high intensity to that of low intensity so that better visual acuity can be attained. Since, as previously stated, functional night blindness is due to a vitamin A deficiency, it seemed only reasonable that attempts to measure dark adaptation should be made and these results used as a test for vitamin A deficiency. Hecht and Mandelbaum³⁷ argued thus:

After the establishment of vitamin A as a factor in the visual cycle, it seemed logical to use the properties of vision for the detection of early stages in vitamin A deprivation.

Hecht³⁸ stated:

Dark adaptation is an expression of the accumulation in the eye of photosensitive substances such as visual purple in the rods and visual violet in the cones. This accumulation of sensitive materials is determined among other things by the vitamin A content of the diet, since night blindness due to dietary deficiency has been cured by the addition of vitamin A to an inadequate diet.

In an attempt to correlate poor dark adaptation and vitamin A deficiency, numerous investigations were undertaken. Frandsen,³⁹ using dark adaptation as a test for mild degrees of vitamin A deficiency, reported that after administration of vitamin A and calcium to 23 patients for one month 11 showed normal dark adaptation. Similar results were reported by Jeans and Zentmire⁴⁰, Jeans, Blanchard and associates,⁴¹ and Caussade, Thomas, Neumann and Davidsohn,⁴² while Jeghers,⁴³ Mathis⁴⁴ and Blanchard and Harper⁴⁵ found a definite relationship

37 Hecht, S., and Mandelbaum, J. Relation Between Vitamin A and Dark Adaptation, *J A M A* **112** 1910 (May 13) 1939.

38 Hecht, S. Vitamin A and Vision, *Arch Ophth* **23** 874 (April) 1940.

39 Frandsen, H. Determination of Hemeralopia as a Test for Mild Degrees of Vitamin A Deficiency, *Hospitaltid (med selsk forh)* **77** 42-48, 1934.

40 Jeans, P. C., and Zentmire, Z. (a) A Clinical Method for Determining Moderate Degrees of Vitamin A Deficiency, *J A M A* **102** 892 (March 24) 1934, (b) The Prevalence of Vitamin A Deficiency Among Iowa School Children, *ibid* **106** 996 (March 21) 1936.

41 Jeans, P. C., Blanchard, E. L., and Zentmire, Z. Dark Adaptation and Vitamin A, *J A M A* **108** 451 (Feb 6) 1937. Jeans, P. C., Blanchard, E. L., and Satterthwaite, F. E. Dark Adaptation and Vitamin A. Further Studies with Biophotometer, *J Pediat* **18** 170, 1941.

42 Caussade, L., Thomas, C., Neumann, N., and Davidsohn, S. Utilization of the Hemeralopia Test for Detection of Vitamin A Deficiency in Children, *Bull Soc d'opht de Paris* **50** 415, 1938.

43 Jeghers, H. The Degree and Prevalence of Vitamin A Deficiency in Adults, *J A M A* **109** 756 (Sept 18) 1937.

44 Mathis, G. Avitaminosis A and Hemeralopia, *Rassegna ital d'ottal* **8** 353, 1939.

45 Blanchard, E. L., and Harper, H. A. Measurement of Vitamin A Status of Young Adults by the Dark-Adaptation Technique, *Arch Int Med* **66** 661 (Sept) 1940.

between vitamin A-deficient diet and poor dark adaptation. Attacking the problem from another angle, Krakov and Semenovskaja⁴⁶ studied the dark adaptation of a patient being treated for cystitis who received no food, and only water, for fifty days. On the forty-fifth day he showed severe night blindness ("hemeralopia"), according to the authors, while two weeks after being on a regular diet the dark adaptation was well within normal limits. Wald, Jeghers and Armínio⁴⁷, Caussade, Thomas, Neimann and Davidsohn⁴⁸ and Mandelbaum and Hecht¹⁰ placed human subjects on vitamin A-deficient diets to study the effect of such diets on dark adaptation, and they came to the conclusion that vitamin A deficiency results in poor dark adaptation. Convincing as these reports may seem, there is much evidence to show that dark adaptation is not a test of vitamin A deficiency. Tansley,⁴⁹ after reviewing the literature up to 1939, expressed great doubt whether dark adaptation curves, as they are usually made, are of any value in detecting slight degrees of malnutrition due to vitamin A deficiency. Nagy and Incze,⁵⁰ following the procedure of Jeans and Zentmire,⁴⁰ examined a series of children in two different schools who were known to receive diets low in vitamin A, and the children in a third school, whose diets were adequate were used as a control. The authors concluded that no differences in dark adaptation could be observed in children who varied widely in their vitamin consumption, while Isaacs, Jung and Ivy⁵¹ found no correlation between dark adaptation and the vitamin A intake of a group of healthy medical students. Since the time of Tansley's⁴⁹ conclusions, in 1939, numerous more carefully controlled investigations have been carried on by Thompson, Griffith, Mutch, Lubbock, Owen and Logaras⁵², Steffen, Bair and Sheard¹¹, Isaacs, Jung and Ivy⁵³, Stewart⁵⁴, Dann

46 Krakov, S. W., and Semenovskaja, E. N. The Influence of Starvation on Visual Function, *Arch f Ophth* **132** 370, 1934

47 Wald, G., Jeghers, H., and Armínio, J. An Experiment in Human Dietary Night Blindness, *Am J Physiol* **123** 732, 1938

48 Caussade, L., Thomas, C., Neimann, N., and Davidsohn, S. Hemeralopia in Induced Hypovitaminosis A, *Bull Soc d'opht de Paris* **50** 276, 1938

49 Tansley, K. Night Blindness, *Brit J Ophth* **23** 161, 1939

50 Nagy, M., and Incze, K. Relation of Hypovitaminosis to Dark Adaptation, *Arch f Augenh* **109** 567, 1936

51 Isaacs, B. L., Jung, F. T., and Ivy, A. C. Vitamin A Deficiency and Dark Adaptation, *J A M A* **111** 777 (Aug 27) 1938

52 Thompson, A. M., Griffith, H. D., Mutch, J. R., Lubbock, D. M., Owen, E. C., and Logaras, G. A Study of Diet in Relation to Health, *Brit J Ophth* **23** 697, 1939

53 Isaacs, B. L., Jung, F. T., and Ivy, A. D. Clinical Studies of Vitamin A Deficiency. Biophotometer and Adaptometer (Hecht) Studies on Normal Adults and on Persons in Whom an Attempt Was Made to Produce Vitamin A Deficiency, *Arch Ophth* **24** 698 (Oct), correction, *ibid* **25** 158 (Jan) 1941

54 Stewart, C. P. Nutritional Factors in Dark Adaptation, *Edinburgh M J* **48** 217, 1941

and Yarbrough⁵⁵, Dow and Steven⁵⁶, Oldham, Roberts, McLennan and Schultz,⁵⁷ and Pollack⁵⁸ Thompson and associates⁵² came to the conclusion

It would appear from our results that neither rate of dark adaptation nor light threshold of the fully dark adapted eye has necessarily a close correlation with intake of vitamin A in the diet. Considerable variation may occur in one individual and between individuals on the same diet.

Dann and Yarbrough's⁵⁵ 2 subjects failed to show night blindness measurable by the dark adaptometer of Hecht and Schlaer after five weeks on a diet deficient in vitamin A. Isaacs and her co-workers⁵³ placed one group of normal adults on large daily doses of liquid petrolatum in an attempt to remove the fat-soluble vitamin A from the food and expel it with the feces. No significant changes in the dark adaptation of this group as compared with that of a control group were found. These investigators then placed 3 subjects on a very low vitamin A diet and found that "a diet containing an average of 74 U S P units of vitamin A daily failed to produce measurable visual evidence or subjective signs of deficiency in 3 subjects maintained on the diet for forty-three to forty-nine days," while 300,000 units of vitamin A daily failed to improve the dark adaptation in some patients suspected of having a vitamin A deficiency. That the adaptometer designed by Hecht and Schlaer is a more reliable instrument for testing dark adaptation than the biophotometer is now generally accepted. Using this newer instrument, Oldham and associates⁵⁷ repeated the work of Jeans and Zentmire^{40a} among school children and came to the same conclusion as did Nagy and Incze,⁵⁰ namely, that there was no correlation between adaptometer readings and the daily vitamin A intake. A number of investigators have shown that many factors other than vitamin A can influence dark adaptation. Stewart⁵⁴ pointed out that fatigue and lack of sleep have an adverse effect on dark adaptation, so also does old age. Pollack,⁵⁸ studying dark adaptation in patients with peptic ulcer, showed that the degree of abnormality bore some relation to deterioration in general condition while McDonald and Adler⁵⁹ have shown that anoxemia

55 Dann, W. J., and Yarbrough, M. E. Dark Adaptometer Readings of Subjects on a Diet Deficient in Vitamin A, *Arch Ophth* **25** 833 (May) 1941

56 Dow, D. J., and Steven, D. M. Investigation of Simple Methods for Diagnosing Vitamin A Deficiency by Measurements of Dark Adaptation, *J Physiol* **100** 256, 1941

57 Oldham, H., Roberts, L. J., McLennan, K., and Schultz, F. W. Dark Adaptation of Children in Relation to Dietary Levels of Vitamin A, *J Pediat* **20** 740, 1942

58 Pollack, H. Metabolic and Nutritional Factors Affecting Dark Adaptation in Peptic Ulcer Patients, *Tr Ophth Soc U Kingdom* **63** 69, 1943

59 McDonald, R., and Adler, F. H. (a) Effect of Anoxemia on the Dark Adaptation of the Normal and of the Vitamin A-Deficient Subject *Arch Ophth*

affects the dark adaptation curve. The truth is that most investigators have lost sight of the fact that tests for dark adaptation are, by their very nature, subjective. The only references to this fact were made by McDonald and Adler^{59a} and by Riddell⁶⁰

Vitamin A Content of the Blood—It followed naturally that when the biochemist developed methods for determining the vitamin A content of the blood this laboratory procedure should be applied to cases of suspected vitamin A deficiency and the results correlated with dark adaptation. Caveness, Satterfield and Dann⁶¹ found only a slight correlation between biophotometer readings and the vitamin A level of the blood, while Bodansky, Lewis and Haig⁶² showed a direct relationship between the vitamin A level of the plasma and vitamin A consumption in infants. By using a special technic for dark adaptation, they concluded that the vitamin A level of the plasma is a considerably more sensitive indicator of vitamin A deficiency than is dark adaptation. "The determination of the level of vitamin A in the blood," stated Goldberg and Schlivek,⁶³ "provides an objective laboratory method of determining whether vitamin A deficiency is present." The work of Haig and Patek⁶⁴ and the results of Steven⁶⁵ also confirmed the earlier reports that no correlation is apparent between dark adaptation and the vitamin A level of the plasma.

Other Tests Closely Related to Dark Adaptation—In 1932 Kiang⁶⁶ reported his observations on the visual fields in patients with various forms of vitamin A deficiency. He studied the blue, red and white fields but could find no definite correlation between the clinical symptoms and the relation of the color fields one to another. However, he concluded that on the whole the contraction, especially of the blue field, is pro-

22 980 (Dec.) 1939, (b) Clinical Evaluation of Tests of Dark Adaptation, *ibid* 24 447 (Sept.) 1940, correction, *ibid* 24 1258 (Dec.) 1940

60 Riddell, W. J. B. Scientific and Clinical Aspects of Night Vision, *Tr Ophth Soc U Kingdom* 63 43, 1943

61 Caveness, H. L., Satterfield, G. H., and Dann, W. J. Correlation of the Results of the Biophotometer Test with Vitamin A Content of Human Blood, *Arch Ophth* 25 827 (May) 1941

62 Bodansky, O., Lewis, J. M., and Haig, C. Comparative Value of Blood Plasma Vitamin A Concentration and Dark Adaptation as a Criterion of Vitamin A Deficiency, *Science*, 94 370, 1941

63 Goldberg, H. K., and Schlivek, K. Necrosis of the Cornea Due to Vitamin A Deficiency. Report of a Case, *Arch Ophth* 25 122 (Jan.) 1941

64 Haig, C., and Patek, A. J. Jr. Vitamin A Deficiency in Laennec's Cirrhosis, *J Clin Investigation* 21 309, 1942, Relation Between Dark Adaptation and the Level of Vitamin A in the Blood, *ibid* 21 377, 1942

65 Steven, D. M. Experimental Human Vitamin A Deficiency, *Tr Ophth Soc U Kingdom* 62 259, 1942

66 Kiang, S. M. Observation on the Visual Fields in Various Forms of Vitamin A Deficiency, *Nat M J China* 18 827, 1932

portional to the other symptoms. Nearly ten years later Rauh⁶⁷ showed that a narrowing of the color field for yellow paralleled the degree of night blindness and in severe cases the field for yellow lay within or crossed the border of the field for green, in 1944 Hamilton, Briggs and Butler⁶⁸ reported a case of partial red-green blindness in which the condition became normal after administration of large doses of vitamin A, only to lapse back to partial red-green blindness when the amount in the blood returned to its original level. Before any of these changes can be accepted as presumptive tests for vitamin A deficiency, many more investigations will have to be made and reported on.

CONJUNCTIVAL MANIFESTATIONS

Biomicroscopy—That the slit lamp and the biomicroscope should be used as a part of the examination when vitamin A deficiency is suspected is self evident, but what changes in the ocular tissues can be accepted as early signs and symptoms of vitamin A deficiency is questionable. In 1941 Kruse,⁶⁹ after having conducted a survey on persons in a low income group, recommended the biomicroscopic examination as a simple, convenient, objective method of detecting early vitamin A deficiency. Berliner,⁷⁰ however, stated the opinion that many of the changes noted by Kruse are common presenile and senile changes, and not signs and symptoms of vitamin A deficiency. Only when more of the early ocular changes noted in cases of vitamin A deficiency are reported on will it be possible to draw definite conclusions.

Conjunctival Pigmentation—In 1931 Pillat⁷¹ reported on a peculiar pigmentation of the conjunctiva produced among Chinese as a result of vitamin A deficiency. The following year similar observations among Japanese who were subsisting on a vitamin A-deficient diet were reported by Matsuoka.⁷² He expressed the belief that this pigmentation is an early sign of vitamin A deficiency. Whether such pigmentation of the conjunctiva occurs among less darkly pigmented races is doubtful.

67 Rauh, W. The Color Field in Experimental Night Blindness, Arch f Ophth **141** 545, 1940

68 Hamilton, W. F., Briggs, A. P., and Butler, R. E. The Testing of Color Vision in Relation to Vitamin A Administration, Am J Physiol **140** 578, 1944

69. Kruse, H. D. The Ocular Manifestations of Avitaminosis A, with Especial Consideration of Detection of Early Changes by Biomicroscopy, Pub Health Rep **56** 1301, 1941, Milbank Mem Fund Quart **19** 207, 1941

70 Berliner, M. L. Early Detection of Avitaminosis A by Gross or Biomicroscopic Examination of Conjunctiva, Am J Ophth **25** 302, 1942

71 Pillat, A. A Peculiar Form of Pigmentation of Conjunctiva in Disease Produced by Vitamin A Deficiency in Adults, Arch f Ophth **127** 575, 1931

72 Matsuoka, H. Histologic Studies on Melanin Pigment in the Conjunctiva II. Pigmentation of the Conjunctiva Following Diseases of Vitamin A Defect, Acta Jap ophth soc **36** 131, 1932

Other Conjunctival Changes—For the accepted conjunctival signs and symptoms of vitamin A deficiency, the reader is again referred to Duke-Elder's¹ "Text-Book of Ophthalmology"

Pathogenesis—The mechanism by which vitamin A deficiency is manifested by the epithelium of the cornea and conjunctiva is not known. Some of the theories are indicated here

1 Desiccation following loss of lacrimation. This theory does not hold, because xerophthalmia may occur with persistence of lacrimation

2 Lack of mucus due to atrophy of the goblet cells in the conjunctival epithelium. This theory has no more to offer than the first

3 Loss of lysozyme in the tears as a result of vitamin A deficiency (Anderson⁷³). The validity of this theory is questionable, because bacterial invasion is not a primary occurrence in xerophthalmia

4 A neurotrophic disturbance. This theory is more satisfactory in explaining the corneal and conjunctival changes than any of the others. In testing the corneal sensibility in cases of vitamin A deficiency John⁷⁴ observed that as the disease advanced to the stage of prexerosis and xerosis the sensibility of the cornea might sink to one hundredth of the normal, while Mellanby⁷⁵ noted degenerative changes in the myelin sheath of the trigeminal nerve in experimentally induced vitamin A deficiency in animals

KERATOCONJUNCTIVITIS SICCA

Occurrence—Keratoconjunctivitis sicca is a relatively rare condition, found most frequently in women at the time of the menopause

Symptoms—The subjective symptoms are those of chronic conjunctivitis, severe photophobia, absence of lacrimal secretion and impaired vision. For a complete account of the symptoms, the reader is referred to Sjogren's⁷⁶ monograph on keratoconjunctivitis sicca. The interesting feature of this condition is that it has much in common with xerophthalmia

Etiologic Factors—Keratoconjunctivitis sicca is generally accepted as a partial symptom of a major syndrome due to a general hypofunction of the glands of internal secretion as a result of the menopause. It is of interest to note that at first Sjogren⁷⁷ felt that he was dealing

73 Anderson, O. Lysozyme in Xerophthalmia, *Hospitalstid* **75** 1029, 1932

74 John, I. Disturbance of Sensibility of Cornea and Conjunctiva in Xerosis and Keratomalacia of Adults, *Arch Ophth* **5** 374 (March) 1931

75 Mellanby, E. Xerophthalmia, Trigeminal Degeneration, and Vitamin A Deficiency, *J Path & Bact* **38** 391, 1934

76 Sjogren, H. Keratoconjunctivitis Sicca, *Acta ophth*, 1933, supp 2

77 Sjogren, H. Keratoconjunctivitis Sicca Partial Symptom of a Major Syndrome, *Arch Ophth* **18** 675 (Oct) 1937, On Keratoconjunctivitis Sicca, *Acta ophth* **16** 70, 1938

with some form of chronic infection, but after further microscopic studies of the lacrimal gland in the initial stage of the disease, he came to the conclusion that the primary and characteristic change in the syndrome is indicative not of a bacterial invasion but rather of a degeneration. In the meantime, Grosz¹⁶ and Lisch⁷⁸ suggested that keratoconjunctivitis sicca might be due to a vitamin deficiency. Gifford^{16b} and Gifford, Puntenney and Bellows,^{16c} although not certain that keratoconjunctivitis sicca is due to vitamin A deficiency, stated that they always prescribed vitamin A for their patients with this condition.

CONGENITAL ANOMALIES

Animal Experiments—In 1935 Hale²⁷ reported his results on the relationship of vitamin A to anophthalmos in pigs.

These studies leave no reasonable doubt that a maternal deficiency of vitamin A will result in a variety of defects in the offspring, including blindness and even a failure of complete development of eye tissues, cleft palates, hare lip, and the arrested ascension of the embryo kidney. The question at once arises as to the relation of these results to various eye defects and weaknesses in the human race. It may be argued that there is a vast gap between pigs and people, but from the biological and nutritional standpoint, the differences are not so great as might appear at first glance. Both are omnivorous mammals with a long gestation period.

It is interesting to note that Warkany and Schraffenberger⁷⁹ produced much the same results in the offspring of rats kept on a diet low in vitamin A.

Human Cases—How frequently vitamin A deficiency will cause ocular congenital anomalies is unknown at the time of this writing. No doubt a study of the problem in those parts of the world where starvation is a commonplace as a result of World War II would produce interesting results.

THERAPY

In the discussions up to this point, I have been concerned with the effects of vitamin A deficiency, and perhaps the impression has been given that deficiency results only from a reduced consumption of vitamin A. It will be wise to consider the other causes of vitamin A deficiency, in order to arrive at a more logical method of treatment.

Reduced Consumption—That a reduced intake of vitamin A if continued over an extended period will result in a deficiency state is general knowledge and needs no further discussion.

78 Lisch, K. Heredity of Sjogren's Disease Associated with Keratoconjunctivitis Sicca, *Arch f Augenh* **110** 357, 1937.

79 Warkany, J., and Schraffenberger, E. Congenital Malformations of Eyes Induced in Rats by Maternal Vitamin A Deficiency, *Proc Soc Exper Biol & Med* **57** 49, 1944.

Defective Absorption—It is obvious that unless the vitamin A consumed is absorbed from the gastrointestinal tract a deficiency state may develop in spite of an adequate diet. Riddell⁸⁰ called attention to this in 1933. He found that definite vitamin A deficiency developed in a case of celiac disease because the patient was unable to absorb the fatty foods, which contained ample vitamin A. Prompt recovery followed when vegetables containing vitamin A were given in amounts sufficient to supply the necessary quantity of this vitamin. Similar results were reported by Wilbur and Eusterman,⁸¹ in whose case vitamin A deficiency developed as a postoperative complication following operation on the gastrointestinal tract, and by Gamble,⁸² in a case of cystic fibrosis of the pancreas.

Uneconomical Utilization—All observers are aware that some internal combustion engines run more economically than others of the same general type, and every horseman will attest to the fact that some animals are much more economical to keep than others. This no doubt also holds true for the human being. That hepatic function may be one of the factors in vitamin A economy is understandable, because the liver, besides being the storehouse for this vitamin, is the organ for converting carotene into vitamin A. This has been pointed out by many observers, among whom are Jeghers,⁸³ Appelmans,⁸⁴ Wolff,⁸⁵ Patek and Haig⁸⁶ and Wohl and Feldman.⁸⁷

Excessive Utilization During Rapid Growth—Since it is generally known that a growing animal, including the human, requires more of all the food elements, namely, proteins, carbohydrates, fats, minerals and vitamins, per unit of body weight than the adult, it will not be necessary to discuss this phase of the problem further.

Excessive Utilization During Severe Illnesses—Any condition which increases the general body metabolism, such as the infectious dis-

80 Riddell, W. J. B. Celiac Disease Associated with Night Blindness and Xerosis Conjunctivae, *Tr. Ophth. Soc. U. Kingdom* **53** 295, 1933.

81 Wilbur, D. L., and Eusterman, G. B. Nutritional Night Blindness. Report of a Case, *J. A. M. A.* **102** 364 (Feb. 3) 1934.

82 Gamble, R. C. Keratomalacia and Cystic Fibrosis of the Pancreas, *Am. J. Ophth.* **23** 539, 1930.

83 Jeghers, H. Night Blindness as a Criterion of Vitamin A Deficiency. Review of Literature with Preliminary Observations of Degree and Prevalence of Vitamin A Deficiency Among Adults in Both Health and Disease, *Ann. Int. Med.* **10** 1304 (March) 1936-37.

84 Appelmans. Xerosis and Hemeralopia in the Adult, *Bull. Soc. belge d'ophth.* **74** 109, 1937.

85 Wolff, H. Ulcer of Cornea and A. Avitaminosis, *Acta ophth.* **16** 323 1938.

86 Patek, A. J. Jr., and Haig, H. The Occurrence of Abnormal Dark Adaptation and Its Relation to Vitamin A Metabolism in Patients with Cirrhosis of the Liver, *J. Clin. Investigation* **18** 609 1939.

87 Wohl, M. G., and Feldman, J. B. Vitamin A Deficiency in Diseases of the Liver. Its Detection by Dark Adaptation Methods. *J. Lab. & Clin. Med.* **25** 485, 1940.

eases, fever, hyperthyroidism and pregnancy, to mention only a few, will increase the need for vitamin A, as well as the other elements of the diet. That such is the case has been shown by the observations of Jegheis,⁸³ Kentgens⁸⁸ and Juhasz-Schaeffer⁸⁹

Therapeutic Methods—*Parenteral Administration* When gastrointestinal disturbances interfere with the proper absorption of vitamin A, parenteral administration of either vitamin A or carotene must be considered. Tai,¹⁴ however, pointed out the contraindication to the use of carotene in hepatic disease, that this is true will be evident if one remembers that the human body cannot utilize carotene as such but must convert it into vitamin A in the liver.

Topical Application The topical application of carotene (provitamin A) in ocular diseases was first reported on by Balachowski⁹⁰ and Ratschewskij⁹¹ in 1934. Two years later Stevenson⁹² recommended the local use of cod liver oil for external diseases of the eye. It was only reasonable that numerous animal experiments with reference to the topical use of vitamin A should be carried on. Such a local use of vitamin A in experimentally induced lesions has been favorably reported on by Rinaldi,⁹³ Heinsius,⁹⁴ Federici,⁹⁵ Vanysek⁹⁶ and Kapuscinski,⁹⁷ but de Rothth,⁹⁸ after several series of animal experiments, concluded that there was no difference in the time necessary for epithelization of the denuded cornea in animals without vitamin A deficiency which were treated with cod liver oil and those treated with liquid

88 Kentgens, S. K. The Relation Between Pregnancy, Disturbance in Dark Adaptation and Vitamin A Content of Blood, *Acta ophth* **16** 332, 1938

89 Juhasz-Schaeffer, A. Hemeralopia in Pregnancy and Vitamin A, *Klin Wchnschr* **17** 407, 1938

90 Balachowski, F. A. Provitamin A as Anti-Inflammatory Factor in Diseases of the Eye, *Sovet vestnik oftal* **4** 470, 1934

91 Ratschewskij, R. A. Physiologic and Therapeutic Action of Colloidal Solutions of Provitamin A in Their Local Application to the Eye, *Klin Wchnschr* **13** 918, 1934

92 Stevenson, E. Cod Liver Oil as Local Treatment for External Affections of the Eye, *Brit J Ophth* **20** 416, 1936

93 Rinaldi, S. Local Use of Vitamins A and D in Treatment of Corneal Lesions, *Ann di ottal e clin ocul* **64** 505, 1936

94 Heinsius, E. Experimental Observations as to the Influence of Vitamin A on Regeneration of Corneal Epithelium, *Arch f Ophth* **136** 103, 1936

95 Federici, E. A and D Vitamins in Corneal Reparative Processes, *Boll d'ocul* **16** 357, 1937

96 Vanysek, J. The Importance of Vitamin A in Regeneration of Corneal Tissue, *Českoslov oftal* **3** 189, 1937

97 Kapuscinski, W. J., Jr. The Action on the Eyes of Rats of a Locally Administered A and the Effect upon This Action of Vitamin D, *Arch f Ophth* **138** 667, 1938

98 de Rothth, A. Local Action of Oils Containing Vitamin A, *Arch Ophth* **24** 281 (Aug) 1940

petrolatum In contradiction to the works of Balachovski and Ratschewskij, Vanysek,⁹⁶ experimenting with rabbits, came to the conclusion that carotene instilled directly into the conjunctival sac produced no beneficial effects on artificially induced corneal lesions In spite of these conflicting reports, Heinsius,⁹⁹ de Grósz,¹⁰⁰ Tikhova¹⁰¹ and many others enthusiastically prescribed local applications of vitamin A in the treatment of such varying conditions as phlyctenular keratoconjunctivitis, trachomatous xerophthalmia, postoperative keratitis, corneal erosion, keratitis neuroparalytica and keratitis bullosa In ophthalmology, as in the other branches of medicine, an understanding of the etiology of disease processes will result in more logical therapy

CONCLUSIONS

1 Hypovitaminosis A may exist in persons who presumably are receiving an adequate diet

2 Even in the absence of demonstrable ocular lesions, poor dark adaptation is not presumptive evidence of vitamin A deficiency

3 Fasting vitamin A levels of the blood are of value as a diagnostic aid in establishing the existence of a deficiency

4 More reports on early ocular changes in vitamin A deficiency need to be made before biomicroscopic examination can be a real diagnostic aid

5 The corneal and conjunctival lesions in vitamin A deficiency are probably neurotrophic, resulting from degenerative changes in the trigeminal nerve

6 Keratoconjunctivitis sicca is probably one of the many ways in which vitamin A deficiency manifests itself

7 Some of the heretofore unexplainable ocular congenital anomalies are undoubtedly due to a vitamin A deficiency in the mother at some critical time during the period of gestation

8 Vitamin A deficiency may be caused by (a) reduced consumption, (b) defective absorption, (c) uneconomical utilization and (d) excessive utilization (1) during rapid growth, (2) during illnesses or (3) during pregnancy

9 Parenteral administration of vitamin A is sometimes indicated

10 Topical application of vitamin A is of doubtful value

441 Lowry Medical Arts Building (2)

99 Heinsius, E Use of Ointment Containing Vitamin A in Ophthalmology, *Munchen med Wchnschr* **84** 936, 1937

100 de Grósz, S Local Use of Vitamin A Preparation in Ophthalmic Practice, *Arch Ophth* **22** 727 (Nov) 1939

101 Tikhova, V A Local Application of Vitamins in Diseases of Eye, *Vestnik oftal* **14** 16, 1939

News and Notes

EDITED BY DR W L BENEDICT

GENERAL NEWS

Home Study Courses, American Academy of Ophthalmology and Otolaryngology—The Home Study Courses in the basic sciences of the two specialties, sponsored by the American Academy of Ophthalmology and Otolaryngology, will be given again beginning Sept 1, 1947. Registrations must be completed before August 15. Detailed information may be secured from Dr William L. Benedict, executive secretary, 100 First Avenue Building, Rochester, Minn.

William Hamlin Wilder Memorial Lecture—Dr John Q. Griffith, Jr., of the Laboratory for the Study of Hypertension, Philadelphia, will deliver the third William Hamlin Wilder Memorial Lecture of The Institute of Medicine of Chicago on Friday evening, May 23, at the Palmer House, his subject being "Rutin: A Therapy for the Hemorrhagic Complications of Hypertension."

Ophthalmological Study Council—The Ophthalmological Study Council will give its third, and last, basic course in ophthalmology at Westbrook Junior College, Portland, Me., June 20 to Sept 13, 1947.

Further information may be secured by writing to the Ophthalmological Study Council, 520 Commonwealth Avenue, Boston.

Stanford University Eye Bank—Officials of Stanford University have announced the establishment of an eye bank, to be located at Stanford University Hospitals, San Francisco. The eye bank, which is under the direction of Dr Dohrmann K. Pischel, will be similar to those now established in New York, Boston and Chicago. A bill now pending will, on passage, make it lawful to will eyes in the state of California.

PERSONAL NEWS

Appointment of Executive Director of the National Society for the Prevention of Blindness—Dr Franklin M. Foote has been appointed executive director of the National Society for the Prevention of Blindness, succeeding Mrs Eleanor Brown Merrill, who is retiring.

Dr Foote was formerly district health officer of the Kips Bay-Yorkville Health District of the Department of Health of New York City. He is assistant professor of public health and preventive medicine at Cornell University Medical College.

A native of Great Barrington, Mass., Dr Foote holds the B.S., M.D. and D.P.H. degrees from Yale University. During World War II, he served as a major in the Medical Corps of the Army of the United States. He is a member of the American Medical Association, a fellow of the American Public Health Association, a member of the Harvey Society of New York City and a member of the New York County Medical Society and the Medical Society of the State of New York.

SOCIETY NEWS

Pan-American Association of Ophthalmology—Officials of the Pan-American Congress of Ophthalmology met in New York in February to discuss matters relating to the Third Congress of the Pan-American Association of Ophthalmology

The date for the Congress has been advanced to Jan 4 to 10, 1948

Regulations of the Congress were adopted by the local committee. Dr Tomas R Yanes, president, Dr Gilberto Cepero, general director, and Dr Miguel A Branly, general secretary

The deadline for receipt of papers and lectures and then accompanying summaries is Aug 27, 1947 (The summaries are limited to 400 or 500 words) Two complete copies must be sent one to Dr Branly, Edificio de la Escuela de Medicina, Calle 25 and I, Vedado, Habana, Cuba, the other, to Dr Conrad Berens, 301 East Fourteenth Street, New York 3, if the author lives north of Panama, or to Dr Moacyr E Alvaro, 1151 Rua Consolacão, São Paulo, Brazil, if the author lives south of Panama The deadline for receipt of the opening discussions on official subjects is August 23, and these must be accompanied with a résumé of 200 to 300 words This date also is the deadline for titles of movies for the cinematographic exposition

Authors wishing to exhibit books, periodicals, etc, must have them in the hands of the local committee by November 30

One entire day will be devoted to a discussion of the prevention of blindness Dr Thomas D Allen, 122 South Michigan Avenue, Chicago 3, was commissioned to direct the instruction courses in English, to be given January 6, 7 and 8, mornings only

Dr Brittain Payne, 301 East Fourteenth Street, New York 3, was commissioned to assemble and direct the scientific exhibit from the English-speaking countries

Dis Payne, Branly and Manoel A de Silva, of São Paulo, were designated assistant secretaries

The program of all the activities of the Congress will close Aug 30, 1947

A copy of the regulations, as well as detailed information on courses, travel, etc, will be sent to all ophthalmologists who by that date have paid their subscriptions

Subscriptions for the Congress are still open Those interested may send a postal order or bank draft for \$10 to Dr Branly, to cover the quota for the Congress If the subscriber is not able to come to Habana, a copy of the transactions, including papers and discussions, will be sent to him when they are published Hotel reservations will be made through Dr Branly at the time of receipt of the fee While subscription fees need not be sent in immediately, hotel reservations cannot be made until they are received, the sooner they are received the easier it will be for the local committee to assign comfortable lodgings

The local committee wishes to send programs, tickets for courses, registration card, name of hotel and number of room, etc, direct to each member as soon as possible

The reservations for travel, transport, etc, may be made through any agency However, arrangements are being made with Mr Harold

E Wright, Atlantic Coast Line Railroad, 217 S E First Street, Miami, Fla, which organization will arrange transportation especially for the Congress and will conduct postconvention excursions at moderate cost

Concerning the commercial exhibition, address Dr Hector Uribe Troncoso, 301 East Fourteenth Street, New York 3, concerning the cinematographic exhibition, Dr Gilberto Cepero, Calle L no 353, Vedado, Habana, and concerning the ophthalmologic literature, Dr Miguel A Branly. Additional information may be obtained by addressing Dr Branly

Reading Eye, Ear, Nose and Throat Society, Reading, Pa—The joint meeting of the Reading (Pa) Eye, Ear, Nose and Throat Society and the Diplomates Association of the physicians of Berks County was held Wednesday, Feb 19, 1947. The meeting was addressed by Dr Eugene P Pendergrass on "Atomic Energy in Medicine"

Correspondence

USE OF EYE BANK EYES FOR TRAINING IN OPHTHALMIC SURGERY

To the Editor —In an article entitled "The Use of Cadaver and Animal Eyes for Training and Experience in Ophthalmic Surgery" (*Am J Ophth* 21 904, 1938), I pointed out that the eyes of recently deceased persons would be most desirable for the purpose. Unfortunately, not until now has there been any possibility of obtaining such material in sufficient quantity. The Eye Bank for Sight Restoration, Inc., may accomplish this. It has the cooperation of ophthalmic surgeons in sending to the bank eyes enucleated from living persons for various pathologic conditions, and, better still, it has prevailed on members of the profession in general, the hospitals and pathologic laboratories and the public to furnish it with the eyes of recently deceased persons. These eyes may be put to good use not only for transplantation of cornea and for research but, in limited numbers at present, for training and experience in ophthalmic surgery.

There are conditions of the human eye that will yield only to surgical measures, and are not amenable to medical or other therapy. The operative procedure must be skilfully and well carried out, with the confidence born of experience. All ophthalmic surgeons must begin and be trained or acquire skill through self instruction. It is then, with expressions of great appreciation that they should welcome the work of the Eye Bank for Sight Restoration, Inc.

There is great sentiment, and justly so, connected with the giving of eyes for corneal transplantation to restore the sight of a blind person. There will be just as great sentiment connected with the giving of eyes for the great, and broader, purpose of saving other eyes by skilful surgery. The legal restrictions and other impediments to this end have been removed. A supplementary clause may be added to the permit for autopsy which will authorize the removal of the eyes for the purposes of the Eye Bank for Sight Restoration, Inc. In case autopsy is not permitted or necessary, the eyes may be given anyway, proper permission being arranged.

I wish to express my personal appreciation of the fine manner in which the material lends itself to demonstration of the operation of intracapsular cataract extraction. Teachers and students have all been disappointed in material heretofore available for the purpose but have made the best of it. Cadaver eyes are too necrotic for any such use, while animal eyes have lenses which are too bulky and zonules which are too resistant and resilient to be of any practical use. Even normal monkey eyes are not adaptable, for the latter reason. Eye Bank eyes, however, are perfect for the purpose. The absence of blood permits the surgeon to proceed with the operation in the cool, scientific manner with which he should work on the living eye. Knowledge of the behavior of human tissues gained in such work will engender a confidence which will help much in carrying through a real operation to a successful conclusion.

The eyes to be suitable must be fresh, and must be available not more than one day after death. The eyes should be from adults, so that the size and shape will be that of the average eye on which the surgeon will operate. Decomposition of tissues, particularly of the uveal tissues, proceeds rapidly after death. It may seem to be wishful thinking that the procedures of obtaining the necessary consent, enucleation of the eyes, refrigeration, delivery to the Eye Bank and, then, distribution and use can be accomplished within twenty-four hours, but I believe that with proper organization and planning this can be done.

A further possible use in the future for Eye Bank eyes is that of serving for examination by the American Board of Ophthalmology for the certification of *safe* ophthalmic surgeons and later, after more extended examination, of *expert* ophthalmic surgeons.

It is for these purposes that I laud the work of the Eye Bank for Sight Restoration, Inc., and trust that it will continue its work as it has been begun, that other organizations will not spring up to duplicate the work and cloud the issue or hamper its development, that colleges and other institutions for training in ophthalmic surgery will join with it and, finally, that members of the profession and the public in general will continue in cooperation and appreciation of the work.

DANIEL B. KIRBY, M.D., New York

Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Bacteriology and Serology

CLINICAL BACTERIOLOGY AND CYTOLOGY OF SOME OCULAR INFECTIONS
C WEISS and M C SHEVKY, *Am J Clin Path* 14: 567 (Nov) 1944

A white man aged 56 had been in an automobile accident in 1941. In July 1943 the right eye was removed because of a "growth". Three months later the patient complained of poor vision in the left eye. Fine deposits were observed on the posterior surface of the cornea and on the anterior surface of the lens. Opacities were present in the aqueous and vitreous. A diagnosis was made of "possible cyst of the retina with retinal detachment and uveitis". The sclera was trephined, and material obtained for culture showed the presence of a yeastlike organism, which was identified as *Toxula histolytica* (*Cryptococcus hominis*).

W ZENTMAYER.

Color Sense

IS IT POSSIBLE TO INFLUENCE CONGENITAL COLOR BLINDNESS? E WOLFFLIN, *Ophthalmologica* 109:324 (June) 1945

The author reviews the work of Studnitz (no references to which are given) on the chemical composition of the material believed to be responsible for the perception of colors. He claims that there are three separate chemical substances, which have different absorption maxima in the various portions of the spectrum, namely in the red, yellow and blue regions. These substances are therefore known as the red, yellow and blue substances. They are found in slight concentration in retinas containing chiefly cones and have been isolated from the oil droplets in the cones of certain animals. Their chemical nature seems to be that of carotenoids. The red substance is recognized as astaxanthin, the yellow substance, as xanthophyll, and the blue substance, as lacertofulvin. At present, these substances cannot be produced in sufficient quantities to test their effectiveness when supplied to the color blind by oral administration, but the author believes that it may be possible to influence color vision by such treatment. No data of any experimental work are given.

F H ADLER

Conjunctiva

CONJUNCTIVAL HEMORRHAGE DUE TO AN INFECTION OF NEWCASTLE VIRUS OF FOWLS IN MAN (LABORATORY AND CONTACT INFECTION)
N I SHIMKIN, *Brit J Ophth* 30:260 (May) 1946

A laboratory assistant, while giving poultry injections for protective vaccination of amniotic fluid from a chicken egg (dilution 1:3,000),

touched the upper lid of the left eye with the forefinger. This was followed by soreness and redness. Later, along the entire length of the eyelid was a subcutaneous hemorrhage, and a heavy subconjunctival hemorrhage covered the upper and outer part of the bulbar conjunctiva. The symptoms disappeared without complications.

W ZENTMAYER

SURGERY OF PTERYGIUM ALTINO VILNURA, *Rev brasil de oftal*
4 188 (Dec) 1945

Paulo Filho's technic of conjunctival autoplasty is described. The author states that he has performed 52 operations of this type and has observed only 3 recurrences. He had always used McReynolds technic but has found that the percentage of recurrences was slightly higher with this method than with that of Paulo Filho.

M E ALVARO

TREATMENT OF GONOCOCCIC CONJUNCTIVITIS AND SERPIGINOUS ULCER OF THE CORNEA WITH SULFONAMIDE COMPOUNDS E WEISZLOVITS,
Ophthalmologica 108 121 (Sept) 1944

Local application of sulfacetimide produced rapid disappearance of the inflammation and the gonococci. In a number of cases of ophthalmoplegia neonatorum the condition cleared up in four to five days, in others, in ten days. The combined local and internal administration of sulfacetimide produced a considerable shortening in the period of treatment. The authors also found that cases of serpent ulcer were favorably treated by combination of the administration of sulfacetimide and "shock therapy" with sulfathiazole.

F H ADLER

Experimental Pathology

RELATION OF THE EYE TO IMMUNITY IN SYPHILIS, WITH SPECIAL REFERENCE TO THE PATHOGENESIS OF INTERSTITIAL KERATITIS
A C WOODS and A M CHESNEY, *Am J Ophth* 29: 389 (April) 1946

A series of experiments indicate that (1) the corneas of rabbits with experimental syphilis do not always share in the immunity to reinfection which develops during the course of the syphilitic infection, (2) direct inoculation of the cornea is followed by the development, in that tissue, of a local resistant state toward the organisms, although in some instances the protection thus conferred is either not absolute or not permanent, (3) vascularization of the cornea appears to be a factor in influencing favorably the development of a local resistant state. It is suggested that the usual late occurrence of interstitial keratitis may be due to a combination of lack of local immunity in the cornea and the occurrence of minor traumatic incidents as the initiating factor. It is also suggested that the healing of the lesions of interstitial keratitis when vascularization occurs is due to the development of a local immunity, presumably through antibodies coming from the blood.

W S REESE

Injuries

PENETRATING WAR WOUNDS OF THE EYE AND ORBIT H H SKEOCH,
Brit J Ophth 29:113 (March) 1945

Military ophthalmic surgery is at present chiefly concerned with penetrating wounds due to high velocity fragment missiles resulting from high explosive action, the cause of 99 per cent of battle casualties and accidents necessitating operation by the military ophthalmic surgeon. The other 1 per cent of wounds are due to flying steel chips resulting from striking cold steel with a steel hammer, the commonest cause of intraocular foreign bodies in civilian life.

Wounds of the eye and orbit due to high explosive action are often multiple, with additional wounds of the head, face, nose and ears, a situation which suggests cooperation in operative procedures on these parts.

After a long trial, the equatorial ring method of roentgenographic localization has proved its worth and is recommended as a routine. The method of removal of foreign bodies by the posterior route is to be recommended because it permits the use of the small electromagnet and provides the nearest and most effective approach of the point of the magnet to the foreign body, and therefore the shortest and most direct line for its removal.

The article is illustrated

W ZENTMAYER

INTRAOCULAR FOREIGN BODY AND SIDEROSIS BULBI W CARVALHO
PINTO and J MENDONCA DE BARROS, Arq brasil de oftal 8:71
(June) 1945

The authors present a detailed case history of an intraocular foreign body which had lodged in the eye a year and a half before examination, the patient having come for an examination because lime had dropped into his eye and vision had decreased. After extraction of the foreign body an operation for cataract was performed a month later. Sena's statistics on the site of penetration, localization and nature of foreign bodies are given. A bibliography is furnished.

M E ALVARO

CHANGES IN THE FUNDUS IN CASES OF MILITARY INJURIES OF THE
EYE O SHERESHEVSKAYA, Vestnik oftal 23:31, 1944

War injuries of the eye are a combination of direct trauma to the tissues and secondary degenerative processes, which appear later and present a varied ophthalmoscopic picture and a difficult diagnostic problem.

Shereshevskaya made examinations in 300 cases for lesions of the fundus after injuries to the orbit and face, general contusions and injuries of the eyeball. Changes in the fundus were found in 76 per cent of all cases of injury of the posterior segment of the eye by fragments and shells. Unilateral changes were found in 68 per cent and bilateral changes in 7 per cent of cases, and in 25 per cent one eye was either enucleated or there were serious injuries of the anterior segment of the eye, followed by blindness.

The choroid was most frequently injured. Ruptures were of varied shapes and sizes, ranging from punctate lesions to ruptures involving

one-half the eyeball, followed at times by massive hemorrhages. The proliferated connective tissue could be mistaken for detached retina, but as a rule with large ruptures of the choroid the exudative inflammation and scarring prevented retinal detachment, only in 2 cases was retinal detachment observed. The secondary changes of choroidal injuries were inflammatory chorioretinitis, ascending atrophy of the optic nerve and degenerative maculitis. Retinal tears were observed less frequently and occurred as holes, mostly in the macular region but at times at the periphery. Retinal detachments were rare.

The macular region was affected frequently as a result of the injury to the choroid and retina and of hemorrhages, and because of the reduction of vision the condition was most serious. In some cases connective tissue formed, and the resulting lesion resembled disciform macular degeneration. Punctate macular hemorrhages were seen often.

Evulsion of the optic nerve was present in 3 cases. In all there were enophthalmos and limitation of motion of the eyeball.

O SITCHEVSKA

Methods of Examination

TECHNICAL REFINEMENTS IN THE REMOVAL OF MAGNETIC FOREIGN BODIES FROM THE POSTERIOR SEGMENT OF THE EYE. G. C. STRUBLE and L. J. CROLL, *Am J Ophth* 29:151 (Feb) 1946

Struble and Croll stress the pinpoint localization of foreign bodies, a painstaking layer dissection of the sclera between scleral retraction sutures and removal of foreign bodies from the posterior segment without penetrating the choroid or pars plana with the magnet tip. The localization is done by means of a small lead plate sewn to the sclera.

W. S. REESE

LOCALIZATION OF INTRAOCULAR FOREIGN BODIES. E. W. PERKINS, *Bull U S Army M Dept* 5:215 (Feb) 1946

No one method of localization of intraocular foreign bodies solves all the problems encountered in battle. Perkins has found the silver wire ring which fits around the equator of the globe to be the simplest method of determining whether or not a deeply embedded foreign body is just within or just outside the eye. It does not give the exact localization so well as the more elaborate methods, but this does not lessen its practical value. The equipment, technic and interpretation of the films are described, and 1 illustrative case report is given. The article is illustrated.

W. ZENTMAYER

UTILIZATION OF THE CAMPIMETER WITH REDUCED ILLUMINATION FOR THE MEASUREMENT OF RETINAL ADAPTATION. R. WEEKERS and F. ROUSSEL, *Ophthalmologica* 110:242 (Nov-Dec) 1945

The state of retinal adaptation alters the position of the isopters considerably when these are measured under conditions of reduced illumination (less than 30 lux). If the rods function normally, one should find a progressive increase in the field of vision under these condi-

tions If the rods are not functioning normally, the field of vision will contract This test constitutes a reliable and sensitive quantitative means of detecting night blindness Quantitative deficiencies, chiefly of proteins and lipids, cause a concentric contraction of the field when the illumination is reduced In order to bring out a scotoma of slight intensity, the field of vision should be measured with reduced illumination, but it is important if one is using this method to appreciate that the state of retinal adaptation tends to alter the position of the isopters and that night blindness can cause a definite contraction of the field under these conditions

F H ADLER

Orbit, Eyeball and Accessory Sinuses

OCHRONOSIS-LIKE PIGMENTATION ASSOCIATED WITH USE OF ATABRINE
[QUINACRINE] H S SUGAR and W W WADDELL, Illinois M J
89: 234 (May) 1946

Sugar and Waddell observed in 10 men who had been treated with quinacrine for considerable periods an ochronosis-like pigmentation never described before These pigmentary deposits are most characteristically seen as a gray-blue discoloration in the bony palate, where it ends as a sharp line at the transition to the soft palate A gray-blue pigmentation of some or all of the nail beds is the next most obvious sign This is manifested either as a transverse band at or near the middle of the nail or as a diffuse discoloration of the entire nail bed The next most obvious finding was pigmentation of the conjunctiva in the area of the palpebral fissure The conjunctival pigment extended in patches of varying size from the nasal and temporal sides of the cornea and involved the corneal limbus nasally and temporally, less frequently below, and in 2 cases involved the plica semilunaris and the caruncle The pigment appeared to lie at varying depths Biopsy in 1 case showed that the pigment lies both in the basal layer of the epithelium and below it This pigmentation associated with the use of quinacrine requires no treatment and is important only in differential diagnosis The pigmentation may cause considerable concern to some patients Among the conditions with which it may be confused are carotenemia, Addison's disease, icteric disease, picric acid poisoning, ochronosis due to phenol poisoning and alkaptonuric ochronosis

J A M A (W ZENTMAYER)

THE FIRST EXPERIMENT IN PROSTHESES OF THE ORBIT MADE OF
PLASTIC MATERIAL D SUDAKEWITCH, Vestnik oftal 6: 43, 1944.

The process of preparing the plastic material for prostheses for the orbit, which was done in dental laboratories, is described in detail These prostheses are light, transparent and of a pleasing color, so that they look natural The prosthesis is held by a wire frame and is attached to the bridge of the frame, and it does not interfere with the movement of the face Three cases of severe injuries of the orbit, involving the zygomatic, the nasal and the maxillary bones, are reported In all these cases the cosmetic result was good Sudakewitch believes

the ophthalmologist should know the technic of the prosthesis, so that he can give certain recommendations to the technician

O SITCHEVSKA

Operations

HETEROGENOUS CONJUNCTIVAL TRANSPLANTATION E ROSEN, Am J Ophth 29: 193 (Feb) 1946

Rosen refers briefly to Filatov's work on grafting animal conjunctiva and summarizes his work. He reports a case in which he used cadaver conjunctiva successfully as a graft in a case in which there was an adhesion between the upper lid and the globe, producing ptosis. He suggests that cadaver conjunctiva in refrigerated or unrefrigerated form may be used in a great many conditions.

W S REESE

PLASTIC EYE IMPLANT A D RUEDEMANN Am J Ophth 29 947 (Aug) 1946

Ruedemann describes an operation in which he implants a plastic globe in the orbit after enucleation. To this he attaches the rectus muscles. Although the procedure is time consuming and difficult, he states that the efforts are justified by the results.

W S REESE

OPHTHALMOPEDICS J J KOHOUT and A CALLAHAN, Am J Ophth 29. 968 (Aug) 1946

Kohout and Callahan describe the use of ophthalmopedics in cases of enucleation and evisceration, contracted socket, wrinkling of the skin complicating lid reconstruction, edema of the lids and ptosis, as an aid in seating abnormally prominent artificial eyes, and in complete loss of eyelids and the orbit. Each ophthalmopedic is first made up in a combination of paraffin and base plate wax.

W S REESE

Physiology

THE RELATIONSHIP BETWEEN LIGHT ADAPTATION AND DARK ADAPTATION AND ITS SIGNIFICANCE FOR APPRAISAL OF THE GLARE EFFECT OF DIFFERENT ILLUMINANTS E SIMONSON, S S BLANKSTEIN and E J CAREY, Am J Ophth 29: 328 (March) 1946

The authors found no consistent relationship between speed of light adaptation and that of dark adaptation. For the speed of light adaptation the duration of exposure appears to be of greater importance than the brightness at low levels of brightness, whereas with higher illumination the brightness is more important. Daily variations of light and dark adaptation do not coincide.

W S REESE

A CENTER FOR OCULAR DIVERGENCE DOES IT EXIST? R G SCOBEE and E L GREEN, Am J Ophth 29. 422 (April) 1946

Scobee and Green review the theory of passive divergence due to elasticity of the orbital structure and put forward further clinical evi-

dence to substantiate it. It would thus seem that the majority of phenomena can be adequately explained on the basis of a single vergence center in the brain (a convergence center)

W ZENTMAYER

Retina and Optic Nerve

A CASE OF ECLIPSE BLINDNESS N A JEVONS, Brit J Ophth 30:84 (Feb) 1946

A man aged 25, on the day following the observation of a partial eclipse of the sun both with and without a protecting screen, mostly with the right eye, found his vision blurred. The only abnormal ophthalmoscopic finding was a circular hole of about $\frac{1}{8}$ disk diameter, with a flat base and steeply sloping sides and surrounded by a zone of edema, visual acuity was 6/18 part. There were an absolute central scotoma of 1 degree and a relative scotoma of 2.5 degrees. There was also a positive scotoma. One month later the only change was the appearance of small, irregular patches of fine pigmentation around the hole.

The article is illustrated.

W ZENTMAYER

A CURIOUS LESION OF THE FUNDUS P PANNETON, Arch d'ophth 5:328, 1945

The author describes the case of a patient aged 44 who came for examination, during the course of which ophthalmoscopic examination of the left eye revealed a whitish mass about one-third the size of the disk in the upper temporal border of the fundus, surrounding the blood vessels. Vision in this eye was 0.9. In an attempt to explain this lesion, the author considers the possibility of tuberculosis, of hyaline deposits, of Coats's disease, of a malignant growth and of congenital anomalies. The patient was otherwise in good health.

L B MARLOW

OGUCHI'S DISEASE, TYPE 1, IN THE NETHERLANDS. REPORT OF THE FIRST CASE J TEN DOESSCHATE, Ophthalmologica 108:1, 1944

This is a review of the literature on Oguchi's disease (congenital night blindness), together with the report of a case. The author criticizes Nakamura's concept of the pathogenesis of the disease.

F H ADLER

TREATMENT OF THROMBOSIS OF THE RETINAL VEINS WITH DICUMAROL J D BLUM and H JEANNERAT, Ophthalmologica 108:129, (Sept) 1944

In 7 cases of thrombosis of a retinal vein—of the central vein in 3 and of branches of the vein in 4—treatment consisted in a combination of dicumarol and heparin. In 2 of the cases roentgen therapy was also given. The authors feel that the results were encouraging and that theoretically this method should offer the best treatment of this condition. In order to avoid complications, they suggest that the patient's prothrombin level be repeatedly determined.

F. H. ADLER

TISSUE THERAPY OF RETINITIS PIGMENTOSA A LIPKINA, Oftal J 2: 29, 1946

Tissue therapy was applied in 30 cases of advanced, long-standing retinitis pigmentosa. The therapy consisted either of injections of aqueous extract of leaves of aloe conserved in the dark, or of injections of this substance combined with implantation of conserved cadaver skin. The time of observation was from six to twelve months. In cases in which five to eight injections of extract of aloe gave no results, implantation of skin was also made. The conclusions are as follows:

1. Injections of aqueous extract of conserved, autoclaved leaves of aloe constitute an effective therapeutic measure in the control of such a severe progressive degenerative process in the retina as retinitis pigmentosa.

2. It is possible through the aid of tissue therapy to obtain improvement of vision, enlargement of the visual fields and usefulness of the worker.

3. The most effective method of treatment was injection of 0.5 cc every other day.

4. The combination of injections of leaves of aloe with implantations of skin was the most effective.

A detailed description of preparation of the leaves of aloe and of the skin is given. Tables illustrate the improvement in vision, visual fields and dark adaptation.

OLGA SITCHEVSKA

Tumors

THE REMOVAL OF ADJACENT NEVI OF THE EYELIDS A CALLAHAN, Am J Ophth 29: 563 (May) 1946

Callahan removed adjacent nevi on the right upper outer margin of lid with a diathermy cutting current and covered both defects with a free graft from the opposite upper lid. Subsequently, an incision was made through the center of the grafted tissue, and another graft from the brow was used to furnish lashes.

W S REESE

CAVERNOUS HEMANGIOMA OF THE ORBIT SUCCESSFULLY REMOVED BY SHUGRUE'S OPERATION M PAUL, Brit J Ophth 30: 35 (Jan) 1946

A Singalese man aged 52 for six months had had progressive proptosis of the left eyeball. At the time of examination the eyeball was almost protruded from the orbit.

Incipient cataract was present. The fundus was normal. A roentgenogram showed no involvement of the cranial bones by the growth. The approach to the tumor was by the Shugrue technic. The tumor was "the size of a marble" and was encapsulated. Microscopic examination showed that the mass was composed of cavernous blood-containing spaces, lined with a well developed layer of endothelium.

The experience with the Shugrue operation in this case suggests that excision of the outer wall of the orbit does not in itself appreciably interfere with the function of the eye nor is the deformity particularly noticeable. The article is illustrated.

W ZENTMAYER

Therapeutics

PENICILLIN TREATMENT OF OCULAR INFLAMMATION I C FRASER
and A A B SCOTT, Brit J Ophth. 30:168 (March) 1946

Of 20 patients with blepharitis treated with penicillin 9 showed apparent clinical cure, and of the others all but 2 were greatly improved, of 4 patients with acute conjunctivitis all were cured, of 6 patients with keratitis or corneal ulceration 4 were cured. Two patients with Eales' disease were not benefited, but it may be worth investigating the use of penicillin in those cases of acute perivasculitis of the retina in which it is thought that a mild septicemia is the cause

W. ZENTMAYER.

PENICILLIN IN OPHTHALMOLOGY Leading Article, Brit M J 1:17
(Jan 5) 1946

While the purulent infections of the outer eye responded readily to general sulfonamide therapy, the intraocular inflammations as a rule responded but poorly. This was particularly interesting, as the sulfonamide compounds easily penetrated into the interior of the eye. The writer states that there is no real clinical support for the observation that the sulfonamide drugs are effective in treatment of infections of the outer eye when used locally and that there is little justification for the widespread and misguided local use of these remedies. Sulfonamide therapy of ocular diseases is thus largely by oral administration of the drug.

Experience with penicillin runs counter to that obtained with the sulfonamide compounds. In contrast, penicillin does not readily penetrate into the interior of the eye when administered intramuscularly. This is a subject which requires further study. For the present it must be accepted that the use of penicillin intramuscularly, in contrast to general sulfonamide therapy, has but little scope in infections of the inner eye. In striking contrast is the local action of penicillin. Since penicillin is not inactivated by pus or peptone, it has proved invaluable in local medication. The limit of local tolerance has been found to be about 2,500 units per cubic centimeter when used in the form of drops. Ointments have not been employed widely, as no adequate base has been available and most of the ointments have been quickly inactivated and have become irritants. Since penicillin fails to pass the blood-aqueous barrier, injection directly into the aqueous and vitreous has been tried, and it has been found that small quantities can be injected without damage. The limit of tolerance of the anterior chamber is about 200 units, and that of the vitreous is perhaps less. It has been found experimentally that the injection of massive quantities of penicillin into the vitreous produces extensive damage. The great difficulty is the maintenance of the concentration. A solution containing 2,500 units per cubic centimeter instilled in the form of drops at intervals of five minutes caused a rapid clearing of the infection in cases of ophthalmia neonatorum.

In conclusion, the article discusses the possibility that penicillin will prove of value in the treatment of trachoma and of ocular syphilis. Little is to be hoped for from the general administration of penicillin in

treatment of ocular diseases, and for the present the scope of the drug is confined to its local use in external infections of the eye

Opinions in the United States are at variance with the writer's on the efficacy of the local applications of the sulfonamide drugs and of the introduction of penicillin into the eye

ARNOLD KNAPP

USE OF PRIVINE IN OPHTHALMOLOGY H ARRUGA, Baicelona, Spain, The Author, 1946

The author refers to the articles on Privine hydrochloride which have emanated from the eye clinics in Geneva and Basel and reports on his own observations Privine is a vasoconstrictor of longer duration but of less effectiveness than epinephrine which is well tolerated and does not cause paralytic vasodilatation It is useful in chronic conjunctivitis, conjunctival hyperemia and allergic and vernal conjunctivitis It is made up in a solution of 1 1,000 and is instilled twice daily, morning and evening

ARNOLD KNAPP

PENICILLIN TREATMENT OF LATE INFECTION FOLLOWING FISTULATING OPERATION G RONNE, Ophthalmologica 111:1 (Jan) 1946

Four cases are reported of late infection following trephination for chronic simple glaucoma in which penicillin proved of value The author advises a subconjunctival injection of penicillin supplemented with instillations The dose should be at least 5,000 Oxford units He believes that the higher the concentration of penicillin and the shorter the intervals between the administrations, the shorter will be the total time of treatment In all these cases cultures and smears may show staphylococci In 1 case of gram-negative micrococcus was also seen Twenty-four hours after the treatment with penicillin was instituted all the cultures were sterile

F H ADLER

TISSUE THERAPY IN TRACHOMATOUS PANNUS D BUSHMITCH, Oftal J 2 22, 1946

Tissue therapy was applied in 33 cases of severe, long-standing forms of pannus which did not respond to any other method of treatment In 30 of these cases there was marked infiltration of the conjunctiva of the lids and fornices

Tissue therapy was carried out in the following manner Subcutaneous injections of 1 cc of extract of leaves of aloe were given every other day, from twenty-five to forty injections being given After the tenth injection, implantation of conserved cadaver skin was made under the skin of the right and left side, with an interval of about a week between the two implantations Locally, the patients were getting only a solution of 0.5 per cent zinc sulfate, in cases of ulceration of the cornea atropine sulfate was used

In the majority of cases the trachomatous process was greatly improved, with decrease in the infiltrations, scarring and clearing of the pannus The ulcers were covered with epithelium after two or three injections of the extract of aloe In 22 cases the time of observation

was from four to ten months. In 43 eyes vision was increased from finger counting to 0.1, 0.5 or 0.8. No recurrence was observed.

Thus, Bushmitch considers therapy with biogenic stimulators very effective in cases of advanced trachoma and pannus.

OLGA SITCHEVSKA

METHODS OF TISSUE THERAPY. TREATMENT WITH BIOGENIC STIMULATORS. V. P. FILATOV, *Vestnik oftal* 25:3, 1946

Tissue therapy is based on the introduction into the recipient's organism of conserved autogenous and heterogenous tissues and of substances of vegetative origin. It originated in Filatov's observation that when additional corneal elements were transplanted around a corneal transplant the corneal tissue conserved at a low temperature acted more favorably on the clearing of the transplant than the fresh cornea.

Animal tissues conserved at a temperature of from 3 to 4 C and leaves of plants kept in the dark, owing to the unfavorable conditions under which they are placed, react in a biochemical reconstruction by producing special substances. Filatov named these substances "resistance substances" or "biogenic stimulators." When introduced into the patient's organism, they stimulate his regenerative processes, increase the cellular metabolism and the physiologic function of the cells and most likely reconstruct the fermentative function of the proteins. This explains why tissue therapy is effective in a wide range of diseases, whether of inflammatory or of degenerative origin. Thus, tissue therapy gave excellent results not only in many ocular diseases—interstitial keratitis, opacities in the vitreous, myopic chorioretinitis, pannus and uveitis—but also in general diseases, such as tuberculosis of the pharynx, contracture of joints, psoriasis, neuritis and various arthropathies. This wide field of action of the biogenic stimulators indicates their non-specificity.

In this article Filatov gives general instructions as to the use of tissue therapy.

Implantation of Tissue—A detailed description of the preparation of the skin of the cadaver and the technic of the implantation is given. The strip of skin with a thin layer of subcutaneous fat, taken from the cadaver, is cut into pieces and placed in a jar in the refrigerator for six days. On the day of the operation, the skin is sterilized in the autoclave at 120 C (1½ atmospheres for one hour). The conserved piece of skin, 6 to 8 cm in size, is implanted into an incised pocket in the patient's skin. The site of implantation may be the abdomen, the thigh or the axillary region. The size of the incision is from 5 to 7 cm. Sutures are applied and removed in a few days. This procedure is simple and painless and may be done on ambulatory patients. A second implantation can be made in two to four weeks. In some cases Filatov combines subcutaneous injections of extracts of conserved tissues with the implantation.

Placenta. Placenta is obtained immediately after birth. A piece is put in the refrigerator for six days, it is then autoclaved, and a piece from 6 to 8 cm is implanted in the same manner as that employed with skin. Similar implantations can be made of testis, muscle, sclera or cornea and of heterogenous material, such as skin, spleen and muscle of animals, which can be obtained at slaughter houses. A small piece of placenta (2 by 2 by 2 mm) can also be implanted into a small pocket.

made in the conjunctiva of the lower cul-de-sac, no sutures are necessary, as pressure on the lips of the wound with forceps for a few seconds will keep the wound closed

Injections—*Extract of Placenta* A piece of conserved placenta is cut into minute pieces and mashed into a cereal-like material To 10 Gm of the latter 100 cc of distilled water is added, the mixture is shaken and kept for one hour at room temperature It is then boiled for one or two minutes in a double boiler The mixture is filtered through a few layers of gauze, heated again to the boiling point and then filtered again through filter paper The filtrate is put into ampules of 1 or 2 cc, the ampules are sealed and sterilized in the autoclave at 120 C for one hour The ampules can be kept in the refrigerator for a few months under routine bacteriologic control Injections of this extract are made subcutaneously daily or every other day, for a total of twenty to thirty injections They can be repeated in one or two months If the injections are painful (usually they are not), 0.5 cc of procaine hydrochloride may be injected previously Similarly prepared extracts of skin, testis, nerve and other tissues can be used for subcutaneous injections Since the boiling, filtering and sterilization deprive the extract of proteins, no anaphylactic symptoms have been observed

Material of Vegetative Origin Leaves of aloe are put on a plate in the refrigerator at a temperature of 4 to 10 C for fifteen days (complete darkness) After this period the thorns are removed, and the leaves are washed and cut into small pieces, placed in jars and sterilized in the autoclave for one hour at 120 C Implantations of pieces of the aloe are made in a manner similar to implantations of skin

Extracts of leaves of aloe are prepared as follows The leaves, conserved in the dark for fifteen days, are cut into very small pieces and then mashed into a soft mixture To 10 Gm of this mixture is added 50 cc of distilled water The solution is kept at room temperature for one hour It is then boiled for one or two minutes, filtered through gauze twice, then boiled for a few seconds again and finally filtered through paper The solution is placed in ampules, which are sealed and sterilized in the autoclave Routine bacteriologic control is observed The ampules can be kept in the refrigerator for five months Injections (1 to 4 cc) are made subcutaneously daily or every other day, until from twenty-five to forty are given The course of injections can be repeated in a month

Tissue therapy has been used widely in the Soviet Union Tissue therapy, Filatov states, "is the general principle of therapeutic medicine," and clinicians can improve on the details as they use it with the various diseases

OLGA SITCHEVSKA

DATA ON TISSUE THERAPY IN THE EYE CLINIC OF THE FIRST MOSCOW MEDICAL INSTITUTE A. CHENTSOV, *Vestnik oftal* 25: 30, 1946

Chentsov tried Filatov's method of tissue therapy in the eye clinic of the First Moscow Medical Institute, chiefly on patients with high myopia and its complications This report is a preliminary and a cautious one, as only 66 cases were observed The author states that more observations are necessary and that for a number of diseases this method may prove as useless as have previous methods Changes

in the macula were seen in 23 cases, hemorrhages in the retina in 5 cases, opacities in the vitreous in 19 cases, detachment of the retina in 3 cases, optic atrophy in 5 cases, uveitis in 4 cases and keratitis in 1 case

Implantation of conserved cadaver skin was used chiefly. In some cases two or three implantations were made. In 3 cases a piece of placenta was implanted under the conjunctiva, but it produced severe irritation of the conjunctiva and was discarded. In six cases the implant did not take, the wound reopened in four to six days, and the implanted skin was "expelled." In some cases preliminary treatment with injections of cod liver oil was given, but in the majority of cases infiltrates formed at the site of the injection, with elevation of the temperature.

In the series of cases of maculitis, there was improvement of vision of 0.1 or 0.2 in 17 cases and no change in 6. In 3 of the cases of hemorrhage into the macula lutea there was some improvement of vision. The best results were obtained in cases of opacities of the vitreous (19), vision being increased from 0.1 to 0.3 in all cases. Of 3 cases of retinitis pigmentosa, there was no improvement in 2, while in the third case vision increased from 0.1 to 0.2 in one eye and the visual fields were enlarged from 10 to 20 degrees in each eye. In cases of optic atrophy and of uveitis there was no improvement, while in a case of interstitial keratitis vision was greatly improved.

The general condition of the patients was notably improved as a result of the tissue therapy, they felt stronger and "younger," and arthritic pain was relieved.

In conclusion, Chentsov recommends the accumulation of more facts and the treatment of more patients with this method, which he regards as a kind of *Reiztherapie*.

OLGA SITCHEVSKA

Toxic Amblyopia

QUININE AMBLYOPIA A BISHAY, Brit J Ophth 30:281 (May) 1946

Within a period of two years Bishay saw 7 cases of quinine amblyopia in a district in upper Egypt, which had a severe epidemic of malignant malaria. The case histories are tabulated. Three important conclusions were reached from dealing with these cases. The amount of quinine that the patient takes need not be large, as described by all other authors. Neither the vascular nor the toxic theory explains all cases, and the author believes that there is another element, i.e., sensitiveness of the patient to quinine. In treatment, paracentesis immediately performed produces best and quickest results.

W ZENTMAYER

Society Transactions

EDITED BY DR W L BENEDICT

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Oct 24, 1946

Burton Chance, M D, *Chairman*

George F J Kelly, M D, *Clerk*

Adenocarcinoma of the Lacrimal Gland Following a Mixed Tumor of Twenty-Five Years' Duration DR I EDWARD RUBIN (by invitation)

Mixed tumor of the lacrimal gland is rare, less than 300 cases having been reported in the literature. It is the commonest disease of the lacrimal gland. The origin of this tumor is not established. Grossly and histologically it resembles mixed tumor of the salivary gland.

The signs and symptoms of mixed tumor of the lacrimal gland are those of a slowly progressive, unilateral, orbital growth. These include proptosis, with displacement of the globe downward and slightly nasalward. A mass felt in the region of the lacrimal gland is a constant diagnostic sign. There are also limitation of motion, diplopia, impairment of vision, fundic changes, lacrimation and exposure keratitis, there is usually no pain.

Recurrence of this tumor is common. The growth is often incompletely removed, and it has a strong tendency to bony invasion. It may become malignant after many years.

Roentgen therapy has little noticeable effect. Surgical removal is the best therapeutic measure and should be as radical as possible. If bone is invaded, it should be resected. If the orbital tissues are involved, immediate exenteration is indicated.

Four surgical approaches are discussed: the direct, the transconjunctival, the Kronlein and the frontal flap, with removal of the roof of the orbit.

A case of mixed tumor of the lacrimal gland in a white man aged 35 was presented. The case had been followed from childhood. At the age of 10 years proptosis was first noted. At the age of 16 years a mixed tumor of the left lacrimal gland was supposedly completely excised. Eleven years afterward the tumor first recurred, and it was excised five years later, at the age of 33. The microscopic diagnosis was "mixed tumor." Within twenty-one months it recurred, and this time it involved the optic nerve, producing papilledema. Intracranial extension was suspected, so a frontal craniotomy, with removal of the roof of the orbit, was performed. This was followed by complete exenteration of the orbit. A large tumor, apparently arising from the region of the lacrimal gland, extended posteriorly to compress the optic nerve. The pathologic report was adenocarcinoma.

In conclusion, I wish to thank Dr Spaeth for the privilege of presenting this interesting and unusual case. I also wish to acknowledge Dr Zentmayer's cooperation in this follow-up report on the case he presented eighteen years ago.

DISCUSSION

DR JACOB H VASTINE II. Dr Rubin has made such a complete presentation of this subject that little remains to be discussed.

Surgical intervention is probably the treatment of choice in cases of mixed tumor, whether of the salivary glands, the nasal accessory sinuses or the lacrimal gland. In some cases operation is impossible or is refused, and in these cases irradiation has value. This may be administered either as roentgen or as radium therapy or as both. The irradiation may be expected to effect regression of malignant tissue and to retard the growth of the benign elements. There is sufficient proof of the value of irradiation to recommend it as a postoperative measure.

It is interesting to note that this patient was first operated on in 1927. He received immediate postoperative roentgen therapy, administered by Dr Henry Pancoast, and did not have a recurrence for eleven years. He was treated by me in 1939 and 1940, and the tumor remained stationary until 1944. He was again operated on in 1944 and at that time received no postoperative roentgen therapy. It is striking that there was a rapid recurrence and that within two years another tumor was removed from the same site. This time it was malignant. The question may be asked whether postoperative treatment in 1944 would have delayed recurrence or malignant change.

Roentgenograms which I made in 1939, and again in 1946, showed pressure erosion of the roof of the orbit in the region of the lacrimal fossa. This defect remained unchanged.

Roentgenograms and photographs were presented of an unconfirmed case in which treatment was carried out by Dr Pfahler and me in 1930. There were marked ptosis and proptosis, which regressed after roentgen therapy alone. The patient had been studied by Dr Goalwine in New York in 1930, at which time a defect in the lacrimal fossa of the orbit was noted. This was similar to the erosion in the case presented by Dr Rubin. That patient was referred to Dr Pfahler for roentgen therapy in 1930. A presumptive diagnosis of mixed tumor of the lacrimal gland was made. Roentgen therapy alone was administered by Dr Pfahler and by me. The patient was entirely well when last seen, five years later.

DR ROBERT A GROFF. In Dr Rubin's case, it was thought prior to operation that the orbital tumor had entered the orbit through the bony defect in the orbital roof seen in the roentgenogram, or that it had extended along the optic nerve into the cranial cavity. When the anterior fossa was explored, there was no evidence of tumor. On removal of the roof of the orbit, it was obvious that the tumor had extended throughout the tissue in the orbit, and it was difficult to identify normal structures. For this reason, I contented myself with excising part of the tumor, with the idea that Dr Spaeth should later remove the entire contents of the orbit.

The procedure of frontal craniotomy and removal of the roof of the orbit is simple and safe. It is done entirely extradurally, so that the subdural and subarachnoid spaces are not entered or contaminated. This method affords excellent exposure of the structures in the orbit, and I commend it not only as an easier means of removing orbital tumors completely but as the procedure for decompression in cases of exophthalmos. The procedure should be carried out jointly by the neurosurgeon and the ophthalmologist. Even though Dr Spaeth has given me the opportunity on many occasions to expose the orbit by this procedure, and I have certain knowledge of the structures within the orbit, I much prefer him, or one of his associates, to do or guide the intraorbital portion of the operation.

DR EDMUND B SPAETH. As soon as I received the report of the biopsy from Dr Groff's transfrontal operation, I did a radical exenteration of the orbit. The reason for the massive and immediate postoperative radium therapy was not the original mixed cell tumor but the report of a clearcut, rapidly developing adenocarcinoma.

My associates and I have another case of mixed cell tumor of the lacrimal gland under observation, and we are wondering, in view of the present occurrence, what is going to happen in that case. In that case operation was performed, using the Kronlein technic, and massive roentgen therapy was given after it. The report we received at the time of the operation, on a frozen section, was mixed cell sarcoma. That is why we proceeded with the massive roentgen therapy. Forty-eight hours afterward a second report was received, and this time it was mixed cell tumor. The young woman had a practically complete ptosis after operation, she refuses operation for this ptosis. I am not urging her. I should much prefer to let that alone for the time being. In this case a sequestrum is developing in the lateral wall of the orbit, and I should not be at all surprised if it becomes necessary to perform a sequestrectomy of that area of the zygoma.

Scleral Necrosis Associated with Periarteritis Nodosa. Report of a Case. CAPTAIN FRED HERBERT (MC), U S N, and LIEUTENANT (jg) SAMUEL D MCPHERSON JR (MC) U S N R (by invitation)

Periarteritis nodosa was first described by Rokitsansky in 1852. In 1866 Kussmaul and Maier described the gross and microscopic pathology of the disease. Since that time more than 550 cases have been reported, and in only 10 per cent of these was ocular involvement exhibited (Urbach, E, and Gottlieb, P M. Allergy, New York, Grune & Stratton, Inc., 1946. Gaynon, I E, and Asbury, M K. *Am J Ophth* 26: 1072-1076, 1943).

Goldsmith has recently reviewed the ocular signs of periarteritis nodosa (*Am J Ophth* 29: 435, 1946). These include papilledema with optic nerve atrophy, involvement of the choroidal vessels, involvement of the retinal vessels with the formation of fusiform aneurysms, retinitis with retinal detachment, hemorrhages and exudates, recurrent hemorrhages of the vitreous and involvement of the extraocular muscles (King, E T. *Tr Ophth Soc U Kingdom* 55: 246-256, 1935. Friedenwald, J S, and Rones, B. Ocular Lesions in Septicemia, *ARCH OPHTH* 5: 175-188 (Feb.) 1931. Goldstein, I, and Wexler, D.

Bilateral Atrophy of the Optic Nerve A Microscopic Study, ARCH OPHTH 18:767-773 (Nov) 1937 Bock, J *Ztschr f Augenh* 78:28, 1932 von Hippel, E *Arch f Ophth* 134:121-145, Bock, J *Ztschr f Augenh* 69:225, 1929) A survey of the literature reveals no report of scleral necrosis occurring in the course of the disease

REPORT OF CASE

G H, aged 31, was first admitted to the United States Naval Hospital, Philadelphia, on April 11, 1946, with the complaint of weakness, headache and anorexia The present illness apparently began two years prior to admission, when the patient, an enlisted man in the Army, had acute otitis media and abscess of the nasal septum While under treatment with sulfonamide drugs, the patient manifested what was thought to be an allergic reaction to them One blood culture out of many made prior to treatment was reported as positive for hemolytic *Staphylococcus aureus* The patient recovered from this acute episode with considerable saddle-back deformity of the nose, due to loss of cartilage, chronic dacryocystitis on the right side, and deafness, necessitating use of a hearing aid In February 1945 he had an interlobar collection of fluid in the right side of the chest and an exacerbation of the chronic dacryocystitis Cultures of the pleural fluid yielded no pathogens, and inoculations of guinea pigs with the fluid were reported to give negative results Both lesions cleared with penicillin therapy, and the patient was asymptomatic until just prior to the present admission

Examination on admission revealed an interlobar collection of fluid in the right side of the chest, chronic dacryocystitis with fistula formation of the right, pronounced saddle-back deformity of the nose, large perforations of the nasal septum and advanced atrophy of all turbinate tissue, with nasal crusting and a tendency toward spontaneous epistaxis The right ear drum membrane was conspicuously retracted, with recent vascularization, and the left drum membrane showed an old perforation with adherence of the margins of the tympanic membrane to the medial wall of the middle ear Repeated examinations of the sputum were negative for tubercle bacilli, and careful study showed no evidence of active pulmonary infection The patient desired a nasal plastic operation, and dacryocystectomy, with excision of the fistulous tract, was performed on May 1, 1946 as a preliminary to rhinoplasty and as a relief measure for chronic conjunctivitis Vision was 20/20 in the right eye and 20/15 in the left eye, and no pathologic condition of the eyes was noted

The immediate postoperative course was uneventful, the wound apparently healed by primary intention, and sutures were removed on the fourth postoperative day At this time edema of the right eyelids developed On the seventh postoperative day there occurred photophobia and lacrimation of the left eye and bilateral superficial punctate keratitis, which persisted in spite of local treatment with hot compresses and intravenous administration of typhoid vaccine On the fourteenth postoperative day a spontaneous subconjunctival hemorrhage developed in the right eye at 1 o'clock, just outside the limbus The following day this lesion became edematous, and a similar lesion appeared in the left eye Within forty-eight hours both lesions ulcerated, and the

patient had spontaneous epistaxis. Smears and cultures were made of material from both lesions and were studied for aerobic and anaerobic bacteria, acid-fast bacilli and fungi. These were all repeatedly negative for organisms except for an occasional colony of diphtheroids. Direct scrapings were taken from both lesions and from the nasal mucosa and stained for tubercle bacilli and the common bacteria. These were likewise negative.

The conjunctival and scleral necrosis continued to progress until a "porcelain white," completely avascular, slough developed. The patient was treated with local application of penicillin drops and systemically with injections of 30,000 units of penicillin sodium every three hours. There was little change in his condition, although twenty-one days after the onset of the ocular disease an occasional vessel could be seen appearing in the area of the slough. One month after the onset the patient was given streptomycin 2 Gm daily for five days, with no apparent effect on the slowly healing process. After cessation of the streptomycin therapy, the patient became febrile, the temperature spiking to 99 to 100 F at irregular intervals. Repeated cultures of blood taken during the febrile period were sterile.

At this time the eyes first showed definite evidence of improvement. Conjunctival epithelium began to cover the scleral sloughs, which had become so deep that uveal pigment could be seen shining through. At the same time, from the marginal conjunctiva, vessels began to invade the sloughing sclera and adjacent cornea to form a superficial pannus. At this time the patient complained of paresthesia in both hands and exhibited persistent eosinophilia, with a count of 8 to 10 per cent, albuminuria (1 to 3 plus), and microscopic hematuria. The sedimentation rate was 27 mm in one hour. The Kahn reaction of the blood was negative, and examinations of the spinal fluid revealed nothing abnormal. In view of these findings, it was thought advisable to perform a biopsy of muscle to exclude periaarteritis nodosa. This was done in the seventh week of the ocular disease.

Pathologic Report (Comdr. T. W. Bennett (MC), USNR) — Sections from the gastrocnemius muscle were studied. In areas in the muscle fibers there was evidence of a low grade inflammatory change. In one area between the muscle fibers there were cross sections of several small blood vessels. These vessels were identified as arterioles. In one vessel, especially, the lumen was practically occluded. The intima appeared to be missing, and there was apparent thrombosis, with beginning canalization. About this area there was proliferation of connective tissue. Adjacent to the narrow area of connective tissue was a zone of round cells, polymorphonuclear leukocytes, plasma cells and occasional eosinophils. In another area there appeared to be complete thrombosis and organization, resulting in fairly dense fibrous tissue. About this area there was evidence of chronic inflammation. In another vessel proliferative changes appeared to be taking place in the intima and the subintimal area. About this area there was a moderate amount of chronic inflammatory change, characterized especially by the presence of plasma cells. It is believed that these sections represent three stages: beginning proliferative changes in the intima, complete thrombosis with occlusion of the vessel and complete thrombosis with beginning canalization of the thrombotic area. These

changes, it is believed, are consistent with those occurring in periarteritis nodosa

In the eighth week of the ocular disease, redness, pain and swelling developed in the right ankle. This was considered to be due to vascular occlusion. This swelling was followed in the tenth week by a similar lesion of the left wrist. The lesion of the wrist suppurated, and exacerbation of the corneoscleral lesions occurred, the necrosis extending into the cornea. Prior to this time the ocular media were clear. Repeated examinations with the ophthalmoscope and the slit lamp failed to show any other pathologic condition. The vitreous now became hazy, and a beam without cells appeared in the anterior chamber eleven weeks after the onset of ocular symptoms. Shallow, necrotic ulcers developed on the buccal mucosa. Multiple vitamins, including riboflavin, failed to influence the course of the disease. Twelve weeks after the onset of ocular symptoms, intradermal nodules developed on both feet and legs. Biopsy of one of these nodules showed typical lesions of periarteritis nodosa. This diagnosis was confirmed by Dr Arnold R Rich, of Johns Hopkins Hospital. Details of the fundus were not visible. The margins of the original scleroconjunctival slough were not healed, but the central portion showed a thin scar with uveal pigment showing through. In the upper margin of the cornea superficial sloughs developed, which coalesced to form an ulcer, with an overhanging edge extending toward the central portion of the cornea in the manner of Mooren's ulcer. There was scattered superficial corneal vascularization. Both corneas became edematous. Several large keratic precipitates developed in the left eye. Vision was 1/200 in the right eye and 2/200 in the left eye.

Because the patient had responded to no other therapy, and in view of the previously reported positive blood culture for *Staph aureus*, the patient was tested intradermally with staphylococcus toxin to determine his sensitivity. He was found to give a mildly positive reaction to 0.1 cc of a 1:1,000 dilution and a strongly positive reaction to 0.1 cc of a 1:100 dilution. With the latter dilution, a superficial slough developed at the site of injection. Intradermal desensitization with staphylococcus toxin in 1:1,000 dilution was given for about a month, with no evidence of favorable response, and he was discharged from the hospital, at his own request, fifteen weeks after the onset of the ocular disease.

A clinically similar type of ocular lesion has been described as anterior metastatic scleritis. According to Duke-Elder (*Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1938, vol. 2, 2062-2063) this is usually due to a staphylococcic embolus (90 per cent), but occasionally to pneumococci. In a few cases no organisms were found.

The fundamental pathologic change in periarteritis nodosa is inflammation of the medium and small arteries with fibrinoid hyaline necrosis and exudative processes. As the necrotizing process subsides in one organ it may involve another, with remissions and relapses. Many etiologic explanations have been suggested, but the most widely accepted one is that it is not a disease entity, but a hypersensitivity of the arterial walls. It is most often related to a bacterial allergy associated with chronic infection, but experimental evidence indicates

that drugs, foreign proteins and serums, and even foods or pollens, may be responsible. Since the widespread use of sulfonamide drugs, the number of cases reported has increased notably.

Hydration Properties of Excised Cornea and Factors Responsible for Transparency DR WILLIAM M. HART (by invitation)

Recent work (Cogan, D. G., and Kinsey, V. E. *Science* 95: 607-608, 1942) has emphasized the degree of hydration as the chief determining factor in transparency of the cornea, and as responsible for the optical difference between cornea and sclera. According to this concept, the cornea is endowed with a dehydrating mechanism to keep down its water content. When this mechanism fails, swelling occurs, and therefore opacification. The sclera, on the other hand, is always opaque because of the absence of any such mechanism. If, however, the sclera is deliberately dehydrated, as by being dried in air or placed in glycerin, it, too, becomes "transparent."

In the present study, swelling and transparency of beef corneas were noted in various buffer solutions, all of which were adjusted to the same osmotic activity (8.94 atmospheres) by adding dextrose. Throughout this study an absolute disparity was found between the degree of hydration and the turbidity of the cornea.

The cornea may be characterized as a lyophilic colloid system, inasmuch as it shows behavior analogous to gelatin and fibrin under like conditions. Like many specimens of gelatin, it has an isoelectric point of p_H 4.6, as shown by the swelling minimum.

Various factors were found to affect the transparency of the cornea independently of the water content. It is suggested that these factors operate by affecting the refractive index of the water or of the micelles or of both.

Affecting the micellar refractive index are the (1) temperature, (2) electrolytes, (3) isoelectric point, (4) dissociation, (5) association, (6) mechanical stresses (as in birefringence), (7) p_H , (8) hysteresis and (9) coacervate formation (due to protein-lipid-carbohydrate complexes). Affecting the refractive index of the water are the (1) p_H , (2) electrolytes, (3) nonelectrolytes, (4) surface tension and (5) temperature. According to this theory, when the refractive index of the solvent water in the cornea becomes very different from that of the particles, turbidity results.

The practical potentialities of these observations were shown in the fact that it was possible to clear the corneal opacities which occur spontaneously in cattle. Further work will be directed toward such an attempt in the intact animal.

DISCUSSION

DR FRANCIS HEED ADLER: It would be difficult for any one to discuss this paper after hearing it for the first time, and it is quite impossible for me to do so, but I cannot refrain from mentioning how delighted I am that work of this type is being done here in Philadelphia. The results of investigations of this character do not remain long in the laboratory. They have definite practical significance.

A few years ago, Cogan, in Boston, and others began experiments on the permeability of the cornea and its property of imbibition, the

results of which are now applied in the clinic. They showed that the normal cornea soon becomes less transparent if bathed with a solution of isotonic solution of sodium chloride or with a hypotonic solution. In order to keep the cornea clear during an operative procedure, such as detachment of the retina, most surgeons now keep the cornea flushed with a saline solution of 1.5 per cent strength. These investigators also showed that most of the deleterious effect of cocaine solutions was due to their being hypotonic.

The question of turbidity of the cornea with loss of its transparency becomes increasingly important with the operation of transplantation of the cornea. For the last few years, Dr. Leopold has been interested in transplanting corneas from frozen dried material. Although these transplants take well, they soon become opaque and remain so. The answer to this is to be found in the kind of work which Dr. Hart is doing, and I trust that he will be encouraged to continue it.

DR WILLIAM M. HART: I wish to thank Dr. Adler for his comment.

As shown in my data, the dehydrated cornea, when rehydrated, is often optically better than normal cornea. I was not aware of Dr. Leopold's work, of course, which was carried on under conditions of war secrecy, but the next point my associates and I had in mind was to try to transplant corneas from the dried state.

Opacity of the cornea is a common condition in cattle. We brought a number of such eyes to the laboratory. Some of them had deep ulcer craters, which I presume would be said to be scar tissue. We could clear such corneas in one of two ways. They could be dried in air, in which case they became clear as normal corneas, or we could let them swell in hydrochloric acid solutions of appropriate strength or in various buffer solutions. Corneas which have been dried may be rehydrated and do not then become opaque again.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Brittain F. Payne, M.D., *Chairman*

Milton L. Berliner, M.D., *Secretary*

Nov 18, 1946

INSTRUCTION HOUR

Malformations and Diseases of the Optic Disk. DR. RALPH I. LLOYD

Dr. Lloyd presented a comprehensive review of cases, illustrated with lantern slides.

OBITUARY

James Watson White, M.D. DR. HAROLD W. BROWN

Dr. James Watson White, long a prominent member of this society, died May 15, 1946, in his seventieth year. In 1905 he received his degree of Doctor of Medicine from Albany Medical College and was in general practice from 1905 to 1913.

Dr. White became associated with Dr. Alexander Duane in 1914 and remained with him until the latter's death, in 1926. The knowledge and understanding of the anomalies of the extraocular muscle which this association offered were soon expressed in Dr. White's authori-

tative discourses on the subject. It was with keen interest and an investigative mind that he continued with this important work and became an international authority on the subject. While Dr. White contributed many important and original observations in his lectures and writings, among which is "Recession of the Inferior Oblique," teaching was his greatest love.

For the past twenty-five years he had spent much of his time in collecting and devising teaching material and in organizing and actively teaching courses on the subject of anomalies of the ocular muscles in various medical societies and hospitals and at his office. He gave freely of his time and knowledge, carrying on an extensive correspondence with his students and colleagues, as a follow-up part of their work with him. He presented this difficult subject in such a vital and understandable manner that his regularly scheduled courses at the meetings of the American Academy of Ophthalmology and Otolaryngology, the New York Post-Graduate Medical School and Hospital and at his office were always in great demand. Many prominent ophthalmologists from every section of the country came to take his work. It was almost solely through his efforts that the important contributions of both Dr. Duane and Dr. White on ocular motor anomalies became of practical use to so many ophthalmologists.

He was a sincere and truly great clinician and teacher, sparing no effort to help the individual student. His now familiar "Dr. White's Diagnostic Card" was originally designed to clarify the diagnostic position of the eyes to a single member of a relatively large class. With students he was practical, patient and considerate and showed an appreciation of their need and an ability and willingness to help. He had the insight and broad, comprehensive viewpoint of a great humanitarian.

As a person, Dr. White was considerate, generous and friendly and possessed a fascinating wit and sense of humor. He had a unique and natural approach to people that was immediately disarming, and he was loved by all who knew him. In the clinics or at his office, the observer never ceased to wonder at the ease with which he immediately gained the affection and cooperation of children. Not only ophthalmologists, but all who had the privilege of his friendship, have suffered a great loss in his death.

REPORT OF CASES

Therapeutic Sulfadiazine Poisoning with Pemphigoid Lesions. Conjunctival Signs DR. BENJAMIN FRIEDMAN

This paper will be published in a future issue of the ARCHIVES

DISCUSSION

QUESTIONS FROM THE AUDIENCE What was the end result in vision? Did the man whose case is described have any record of inoculation? Were any cultures made of the contents of the vesicles? Did the question of smallpox arise during the examination?

DR. BENJAMIN FRIEDMAN The conspicuous feature of these cases was that the cornea was never attacked. For that reason, the end results were easy to distinguish from those of trachoma, in which the cornea becomes involved and vision is often affected. Likewise, it differentiates this disease from the particular type of erythema

(Stevens-Johnson disease) which affects the cornea in a severe manner. The condition in these cases was not the result of smallpox. The cutaneous lesions were described by the dermatologists as characteristic of pemphigus. In all the cases a misdiagnosis either of measles or of scarlet fever was made. That, of course, is easy to do in a large military establishment, because the personnel are primarily on guard against contagious diseases, and when there is any rash which simulates a contagious disease the patient is immediately treated for such. The longer these patients were treated with sulfonamide drugs the worse they became, and this particular patient nearly died as a result of the drug poisoning. The Navy reserves the name of therapeutic poisoning for cases in which there is an untoward reaction to any drug.

Fundus Oculi as an Indicator of Vascular Damage in Diabetes Mellitus DR HENRY DOLGER

The twenty-five years since the discovery of insulin have witnessed a mounting incidence of degenerative changes in all diabetic patients. Wagener reported a "steadily increasing frequency of retinopathy, especially in the younger age groups" (in 76 per cent of patients under 30 who had had diabetes more than ten years).

His claim that the duration of diabetes is more important than the age of the patient is corroborated in the present study. Careful scrutiny of the retina of each patient over the course of years indicated that the earliest clinical manifestation of vascular damage can be found in the eye. This was especially true in 55 patients with "juvenile diabetes" in whom hypertension and albuminuria were noted after the typical retinal hemorrhage had occurred.

Within a period of a twenty-five years' duration of diabetes, not 1 of 200 patients examined regularly escaped retinal hemorrhage, regardless of age of onset, severity of diabetes or type of treatment used.

Retinopathy usually presaged progressive vascular degeneration. Fifty per cent presented hypertension and albuminuria at the time of the earliest retinal hemorrhage.

Present day treatment of diabetes has failed to avert the accelerated vascular damage which is an associated phenomenon of the disease, and not a "complication."

DISCUSSION

DR BRITAIN F PAYNE As diabetic hemorrhage is a matter of general concern to ophthalmologists, may I ask what effect, if any, does vitamin C have on the absorption of diabetic hemorrhages?

DR CONRAD BERENS Has Dr Bolger had any experience with vitamin P (rutin, hesperidin)? I have wondered whether patients who showed increased capillary fragility might be benefited, whereas those who did not show increased capillary fragility might fail to be benefited.

DR MARTIN COHEN Has Dr Dolger had any experience with lipemia retinalis, which is pathognomonic of diabetes, and how does he account for the fact that there are no hemorrhages in this condition and no degeneration of the vascular wall? Is the latter condition the factor?

DR JOSEPH J FRIED Did Dr Dolger mention the diagnostic importance of capillary aneurysms and phlebosclerosis as the first manifestations in the eyegrounds in cases of diabetes in which there are no hemorrhages? This is thought to be of considerable importance from the diagnostic and the prognostic point of view, as these signs point to general vascular damage before any routinely known signs of diabetic retinopathy are present

What is Dr Dolger's clinical experience in such cases? Also, what is his experience with hesperidin—vitamin P, or recently better known as rutin? This therapy was lately recommended in cases of diabetic retinopathy to counteract increased capillary permeability and increased capillary fragility

PROF W J B RIDDELL, Glasgow, Scotland I have nothing to add, except to refer to the work of my predecessor in Glasgow, Professor Ballantyne, who has been interested for many years in diabetic retinitis Dr Fried has spoken of the aneurysms, which Dr Ballantyne was the first to describe, and as to the significance of which I think we agree

DR HENRY DOLGER Vitamin P, "citrin," rutin and hesperidin are similar substances, flavone glucosides of varying degrees of purification Neither vitamin C nor vitamin P, rutin nor hesperidin influenced retinal hemorrhages significantly and unequivocally Evaluation of such therapy is difficult because of the spontaneous remissions and exacerbations displayed by these lesions The retinopathy is not a vitamin deficiency but a fundamental alteration of the intracellular oxidative enzyme systems The work being done with cytochrome C, or related oxidative enzymes, by which one is able to maintain the visual threshold during anoxia, is far more provocative and pertinent than vitamin research Because of this more promising approach, I have given up hope in the use of rutin and hesperidin with vitamin C My results with these agents have not been strikingly different from the spontaneous improvement often shown by a group of untreated control patients Whether vitamin C is given by intravenous injection or orally seems immaterial A number of these patients have had repeated determinations of the ascorbic acid level of the blood and, although no value was below normal, the lesions recurred or disappeared without any evidence of vitamin C deficiency

This brings up the question of capillary fragility The tourniquet test has no bearing on the ocular lesion In patients with normal or high vitamin C levels of the blood in whom I could observe the appearance of repeated hemorrhages, the capillary fragility test proved so variable as to be valueless It might be positive one day, negative within twenty-four hours and positive again a week later The erratic behavior of the tourniquet test week after week in the same patient could not be correlated with associated changes in the retina In the main, as the retinal lesions advanced inexorably, the test remained positive despite intensive therapy I do not believe that the tourniquet test measures anything but the integrity of the intercellular cement in capillary walls, and therefore more delicate alterations of function in these structures cannot be estimated by present methods

Lipemia retinalis has nothing to do with this vascular lesion. It is a hang-over from the days when patients were on high fat diets and lipemia was more common. The lesion I am discussing is a vascular one and is related to the capillary aneurysms described by Ballantyne. I feel that this controversy of whether or not aneurysms exist has almost a religious bias. I believe that persons who are unbiased and who examine the eyegrounds repeatedly and early cannot help but find them, especially in younger patients with diabetes of some duration. Except for the occasional chance finding of the early lesions of capillary aneurysm and retinal hemorrhage, the ophthalmologist is privileged to see only the later stages of diabetic retinopathy. Only by the diligent and repeated scrutiny of the retina throughout the course of the diabetes will the true pathogenesis of this tragic complication be understood.

PAPER OF THE EVENING

Hereditary Anomalies of the Eye (Charles H. May Memorial Lecture)

PROF. W. J. B. RIDDELL, Glasgow, Scotland

This general title has been chosen to cover a few of the common hereditary anomalies of the eye in which I have been interested as a clinician. Certain conditions, such as color blindness, are clearly hereditary and are not influenced by the environment of the patient. Myopia is probably under more genetic than environmental control, whereas infections are conditioned to a greater extent by environment, but families with low resistance to common infections are well known. Injuries are largely due to environment, although persons with blue scleras are more liable to break their bones than are normal people.

Modern genetic theory is a particulate one, concerned with the twenty-four pairs of chromosomes which are known to exist in man. The determining factors or genes are assumed to exist within the chromosomes like beads on a string. Two conditions having no pathologic connection, such as hemophilia and color blindness, may be inherited through genes carried on the same chromosome or on opposite members of the same pair of chromosomes. I have traced out the segregation of these two anomalies in certain families. The pooled data from other such pedigrees have made it possible to express the position of the genes as a linkage relation. Recent work has added considerably to knowledge of this problem, and it is now possible to envisage the creation of human chromosome maps. The collection and publication of material suitable for such studies may add to scientific knowledge, and it is a field open to any trained clinician, in fact, he may be at a greater advantage in such work than a pure scientist.

Book Reviews

Optical Transplantation of the Cornea and Tissue Therapy By Academician V P Filatov Price, 31½ rubles Pp 232 Moscow Markomzdiav, State Publishers of Medical Literature, 1945

This book by the distinguished Russian pioneer in corneal transplantation is a summary of his previous work on corneal transplantation and tissue therapy. It is divided into two parts (1) corneal transplantation and (2) tissue therapy.

In the first part he discusses the history of keratoplasty, the classification of corneal transplantation according to the therapeutic requirements, the condition of the leukoma and the indications for and the technic of partial penetrating corneal transplantation. The Filatov-Maizinkowsky trephine is described, with illustration, and its advantages are evaluated. A special spatula connected with Filatov's trephine prevents the injury of the lens and prolapse of the vitreous. The complications (of which the most frequent is glaucoma in the postoperative period) and the material for corneal transplantation are discussed in another chapter. Filatov has been using material from the cadaver, the eye being enucleated two to twelve hours after death and preserved at a temperature of 2 to 4 C for from one to three days.

A total of 842 keratoplasties were performed by Filatov and his co-workers from 1922 to 1941 (a number of transplantations done during wartime are not included). In 171 operations the cornea was taken from the living person and in 671 from the cadaver. Successful results were obtained in 24.1 per cent of the first series (cornea from the living eye) and in 66.6 per cent of the second series (cadaver cornea). (These data include favorable cases only.) The author thus prefers the use of preserved cornea from the cadaver because of the better results. He states that corneal transplantation has proved that homoplasty in the human cornea is possible. Improvement of the leukoma by additional transplantation of transparent corneal elements is the content of another chapter. Filatov believes that this improvement is brought about by rearrangement of the corneal elements and that clearing of the leukoma is effected by biogenic stimulation.

The experimental and pathologic study of the transplant occupies an important place at the Odessa Experimental Institute of Ophthalmology (some eyes with corneal transplantation were removed after the death of the patient, and some eyes were enucleated because of painful glaucoma). This investigation indicates that a true union of the transplant takes place and that regeneration of the corneal elements from the periphery of the cornea does not occur. A study was made of the corneal transplant, its nutrition and the effect of preserving it at various temperatures and in various mediums. It was found that the cornea was preserved best per se, without any fluids, at a temperature of 3 C. It was also found that the oxidation processes were preserved both in the cornea and in the lens, i e., despite the autolysis,

the viability of these tissues was maintained. The cornea preserved at a temperature of 2 to 4 C showed a direct division and growth of the cells, i e, growth of corneal cells in the tissue was obtained at a low temperature, constituting a new phenomenon.

One hundred and thirty-four photographs illustrate the favorable results of keratoplasty with use of cadaver cornea preserved at a low temperature. Vision was improved in the eyes so treated from counting fingers to from 0.03 to 1.0. The time of observation was from seven months to three or four years.

In the second part, tissue therapy is discussed. Tissue therapy took its origin from keratoplasty. In 1933 Filatov began to use transplantation of clear corneal tissue when the transplants became opaque and obtained a clearing of the original transplant. He uses the cornea preserved at a low temperature, as such transplants evidently contain substances which stimulate and accelerate the regenerative power of the corneal tissue of the recipient. He emphasizes the use of preserved tissue as essential and as the basis of tissue therapy. Filatov explains the salient points of tissue therapy as follows:

Under certain conditions any animal tissue undergoes biochemical transformation and forms active substances, which Filatov calls "resistance substances," or "biogenic stimulators." These substances stimulate biochemical processes in the tissues in which they develop. Low temperature appears to be an unfavorable condition for animal tissues and darkness for green leaves. Thus, tissues preserved at a low temperature or leaves of aloe kept in darkness for fifteen days are rich in biogenic stimulators. If such tissue is introduced into the affected organism (by implanting a piece subcutaneously or injecting an aqueous solution), it stimulates the regenerative qualities of the organism and increases the cellular metabolism, and thus aids the recovery of the organism.

Filatov and his co-workers have been using the following tissues: cornea, conjunctiva, skin, placenta and extracts of placenta, as well as injections of cod liver oil. Leaves of aloe preserved in the dark for fifteen days at a low temperature is the plant tissue used. These tissues sterilized in the autoclave at a temperature of 120 C for one and one-half hours do not lose their biogenic stimulating quality. The tissues are implanted either under the conjunctiva or into the skin of the abdomen. Cod liver oil is given intramuscularly, 1 to 2 cc every other day, for from ten to fifteen injections.

Tissue therapy was applied in a great number of diseases of the eye, namely: opacification of the transplant, 16 cases, interstitial, tuberculous, scrofulous, rosacea and herpetic keratitis, 117 cases, corneal ulcer, 23 cases, uveitis, 23 cases, and retinitis pigmentosa, 110 cases. In cases of the last condition injections of cod liver oil, implantation of preserved liver tissue into the skin or implantation of placenta under the conjunctiva was used. In 180 cases of trachoma and in a number of cases of optic nerve atrophy tissue therapy was of benefit. The best results were obtained in cases of keratitis and uveitis.

Tissue therapy was also applied in relief of various other diseases, such as lupus of the skin of the face and mucous membranes and

psoriasis. In all these cases the disease was of long standing and did not respond to routine therapeutic measures. Good results were obtained with inflammatory conditions of the female pelvis and its organs. Tissue therapy gave beneficial results in cases of poorly unified fractures of bones, contractures of joints, tuberculous arthritis (without fistulas), inflammation of the sacroiliac joint and myositis.

The book contains a wealth of material, with histories and photographs of patients and illustrations of the technic.

A great deal of experimental work has been done, and such investigations are still going on in several laboratories for the evaluation and improvement of methods of tissue therapy. This book does not lend itself to abstracting, particularly the experimental parts. A translation would be useful for the English-speaking ophthalmologist.

OLGA SITCHEVSKA

Ocular Prosthesis By J. H. Prince Price, \$4 Pp 184, with 71 illustrations Baltimore Williams & Wilkins Company, 1946

The production and fitting of ocular prostheses have become more important with the introduction of new materials and with an increase in the need of artificial eyes. A quarter of a million people in this country wore prostheses before the war, and the number has significantly increased. This monograph, written by a member of the British Optometric Society, is a summary of earlier methods and a brief introduction to improved forms made possible by chemical advances.

The first seven chapters discuss the history of artificial eyes, the anatomy and physiology of the orbit and clinical fitting. The final chapter is an elementary presentation of the materials and methods of manufacture.

Polished stone or gold implants were originally used. These were chemically and esthetically unsatisfactory and were rapidly replaced with the introduction of glass, made in molds or by blowing. Various formulas have been used in making glass that is durable, colorable and resistant to tears and the secretions of the residual mucous membrane, silicon dioxide is mixed with varying amounts of common light metals and with aluminum, lead, fluorides or titanium for resiliency and tinting.

Since glass is breakable and difficult to manufacture in a large series of colors and sizes, plastic materials have lately been used. Methylmethacrylates, of the acrylic ester group, have proved most successful. In actual manufacture, a mold of the indicated size is made with dental stone and placed in a press. Acrylic monomer and polymer, with suitable colorings, are mixed, placed in the mold and heated. An iris is then put on the scleral shell with paints or by photogravure, and a cornea of clear acrylate is added. Such a prosthesis is light, relatively immune to ocular secretions and esthetically pleasing.

The presentation is uneven both in its clinical and in its manufacturing aspect, for example, there is no mention of spontaneous explosion of glass eyes, sympathetic ophthalmia or basket implants. Nonetheless, this small book is an informative introduction to a subject of increasing significance to ophthalmologists.

LLOYD MILLS JR

SYMPTOMATOLOGY OF SUBDURAL HEMATOMA IN INFANTS AND IN ADULTS

Comparative Study, with Particular Reference to the Ocular Signs, an Observation
Concerning Pathogenesis of Subdural Hematoma

CLIFTON D GOVAN Jr, M D

AND

FRANK B WALSH, M D

BALTIMORE

THE SYMPTOMS of subdural hematoma in adults are quite different from those which occur in infants. The differences in the ocular signs in patients of these age groups suggested this study. Post-mortem examination of infant and adult brains led to an observation which seems to explain important differences in symptomatology.

The first part of this paper concerns symptoms and is based on personal observations and studies on 37 infants and 54 adults. Particular attention has been given to differences in symptoms, both general and ocular, in infants and in adults. The second part records an anatomic observation which may explain differences in manifestations in the two age groups.

TERMINOLOGY

Subdural Hematoma—This term describes any collection of blood in the subdural space, whether or not it is encapsulated. Obviously, in cases in which operation is undertaken immediately after an injury there has not been sufficient time for encapsulation to occur. Little is added by subdividing subdural hematomas into acute and chronic types.

Subdural Hydroma—This term is applied to subdural accumulations of fluid which may or may not contain a small amount of blood. If the amount of blood present determines the connotation of "subdural hematoma" or "subdural hydroma," it is obvious that in many instances either term would be proper. However, subdural hydroma may result not only from trauma (the usual cause of subdural hematoma) but also from extradural infections, sinus thrombosis, meningitis and hydrocephalus, consequently, the character of the subdural fluid may vary within wide limits. Usually it has a higher protein content than the

Read at a meeting of the College of Physicians of Philadelphia, Section on Ophthalmology, March 21, 1946

From the Department of Pediatrics of the Johns Hopkins University, and the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital

were present in 10². Among the poorly nourished infants evidence of infection of one type or another was frequently present.

Convulsions—Convulsions were present in 28 infants (and absent in only 7). This is in contrast to the adult group, only 2 of whom had convulsions. In infants the convulsions were frequently generalized, but in some instances they were localized to one side of the body or face. Ingraham and Matson³ drew attention to tetany due to low calcium metabolism and fever which sometimes obscured the true cause of the convulsions. In infants a convulsion was frequently the first evidence that anything was wrong.

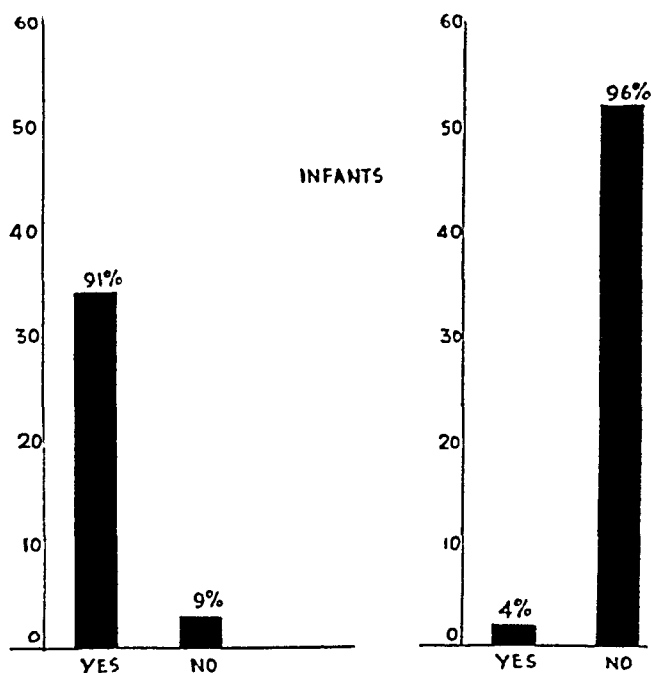


Fig 4—Incidence of history of convulsions in infants and in adults with subdural hematoma

Vomiting—This was present in 18 (about half) of the infants and in 16 (approximately a third) of the adults. The difference in the two series of patients was not sufficient to be noteworthy.

Sensorium—Drowsiness with retained irritability to stimulation was present in 20 infants to a pronounced degree. Only 2 of the 36 infants were "alert." In adults drowsiness, with or without irritability, was an extremely common symptom. The drowsiness merged

2 The sections of bones were reviewed by the late Dr Samuel Blackman, of the department of pathology of the Johns Hopkins University.

3 Ingraham, F. D., and Matson, D. D. Subdural Hematoma in Infancy, *J. Pediat.* 24 1-37, 1944.

into coma in a number of cases. Nine infants (one fourth) and 19 adults (roughly one third) were comatose when first examined.

Bulging Fontanel and Enlargement of the Head in the Infant—Bulging of the fontanel was exceedingly common, 26 of the 28 infants with an open fontanel exhibited the sign. When the fontanel was open, this sign was practically constant.

Fever—Twelve of the 36 infants on admission showed an elevation of temperature to 38 C (100.4 F) or above. We do not have accurate figures on the adult patients, but in the acute stages fever may be expected.

Neurologic Signs—In many adults and infants definite neurologic signs were absent. As already mentioned, a common feature in most

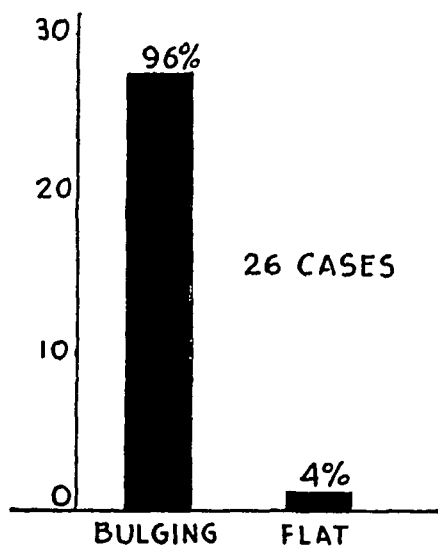


Fig 5—Incidence of bulging fontanel in 28 infants with subdural hematoma

patients was increased irritability and drowsiness. The ocular signs of importance—pupillary dilatation, retinal hemorrhages and papilledema—and their significance are considered subsequently.

In 51 adults the hematoma was unilateral, and hemiparesis was present in 22. In 17 patients the weakness was contralateral to the lesion, and in 4, ipsilateral. In 1 patient hemiparesis was present when the hematoma was bilateral. Hemiplegia ipsilateral to the hematoma is explained on the basis of pressure of the tentorium on the opposite side of the displaced brain stem. The hemiparesis was associated with tendon hyperreflexia, the Babinski sign and ankle clonus. The hemiparesis usually developed late, was rarely complete and varied in severity from time to time. In a few instances the paresis was flaccid.

In infants, from the standpoint of diagnosis, the neurologic signs were of secondary importance to bulging of the fontanel. Blood in the

spinal fluid and drowsiness. However, in their essential features they were the same as in adults except that the signs were usually bilateral.

Spinal Fluid—In infants the spinal fluid invariably contained blood or was xanthochromic. In the great majority of adults the spinal fluid was normal.

OCULAR SIGNS OF SUBDURAL HEMATOMA

Subdural Hematoma of the Optic Nerve Sheaths—This condition, although not described here in any detail, deserves mention. A brief statement regarding the disposition of the dura mater in the optic canal and orbit is necessary to an understanding of it. The dura mater which surrounds the brain and is attached to the skull is continuous about the optic nerve, which it reaches at the entrance to the optic canal. As the optic nerve passes toward the eye through the canal it is surrounded by dura, which is loosely attached to the bony walls of the canal and to the optic nerve. When the anterior orbital opening of the canal is reached, the inner portion of the dura continues about the optic nerve to the posterior surface of the eyeball. The outer portion of the dura leaves the optic canal to become the periorbita. Because there is no real subdural space in the optic canal it is obvious that a subdural hematoma within the orbit is unlikely to extend into the cranium. Also it seems unlikely that a subdural hematoma within the cranium would extend into the orbit, although Liebreicht⁴ suggested that subdural hematoma of the optic nerve sheaths might develop as a result of blood passing along the fluid spaces about the ophthalmic artery into the orbit. He demonstrated a lack of continuity between subdural accumulations of blood within the orbit and those within the cranial cavity.

We are unable to state precisely the ocular signs of orbital subdural hematoma because a great majority of persons who have such a lesion exhibit signs which are in general attributed to injury but are not considered as indicating operation. Our clinical studies point to absence of orbital subdural hematoma in cases of intracranial subdural hematoma. It is of interest that subarachnoid hemorrhage within the cranium is frequently associated with a similar accumulation of blood within the orbit. This is in sharp contrast to what prevails with subdural hematoma. Probably subdural hematoma of the optic nerve sheaths occurs not uncommonly with subarachnoid hemorrhage, both intracranial and intraorbital.

Intracranial Subdural Hematoma—The ocular signs in infants and in adults are quite different, and the differences are important.

⁴ Liebreicht, cited by Cone, W., and MacMillan, J. A., in Penfield W. *Cytology and Cellular Pathology of the Nervous System*, New York: Paul B. Hoeber, Inc., 1932, vol. 2, pp. 848-850.

Papilledema—The occurrence of papilledema in adult patients has been estimated by several observers to be about 50 per cent (Dandy,⁵ Kunkel and Dandy,⁶ King,⁷ Furlow⁸) This figure seems high on the basis of our observations It is also high according to the case records we have used in the preparation of this paper We found mention of papilledema in approximately 17 per cent of both the adult and the infant patients

The papilledema seen in adults is precisely similar to that which is observed in many cases of cerebral tumor, that is, there are varying amounts of swelling of the optic disks, and there may or there may not be retinal hemorrhages of nerve fiber layer type The papilledema which is sometimes seen in infants is, according to our experience, almost invariably associated with subhyaloid retinal hemorrhages In both infants and adults, long-standing papilledema is likely to be associated with optic atrophy of the nerve and loss of visual acuity It is our belief that papilledema is a late development in these patients

Retinal Hemorrhages—In the series here reported the frequency of subhyaloid (preretinal) hemorrhages in infants and their uniform absence in adults are both noteworthy and difficult to explain In this regard, it is again remarked that in infants there usually is blood in the spinal fluid (or xanthochromia) and that the spinal fluid in adults is clear It is generally believed that subhyaloid bleeding is venous in origin, but the exact mechanism responsible for the production of preretinal hemorrhage is unknown Perhaps there are episodes of relatively greater and more sudden increases in intracranial pressure in infants than in adults We have come to believe that in a healthy infant the presence of subhyaloid (preretinal) hemorrhage almost certainly indicates a subdural hematoma In an adult the presence of such a hemorrhage almost rules out subdural hematoma

Pupillary Signs—Careful observation of the state of the pupils is of the greatest possible importance, particularly in adults It is of less significance in infants because in them the lesion usually is bilateral In adults one pupil may be dilated and fixed, or relatively fixed, to light on the side of the lesion Infrequently the pupil contralateral to the lesion is dilated Dilatation of the pupil may be transitory and

5 Dandy W E Subdural Hematoma, in Lewis, D Practice of Surgery, Hagerstown, Md, W F Prior Company, Inc, 1932, vol 12, pp 848-850

6 Kunkel, P A, and Dandy, W E Subdural Hematoma Diagnosis and Treatment, Arch Surg 38 24-54 (Jan) 1939

7 King, C Chronic Traumatic Subdural Hematoma as a Cause of Choked Disc, Tr Am Ophth Soc 63 732-742, 1936

8 Furlow, L T Chronic Subdural Hematoma, Arch Surg 32 688-708 (April) 1936

slight. Such dilatation, according to Woodhall and his associates,⁹ is as significant from the viewpoint of localization as more prolonged dilatation.

We are in complete agreement that unilateral dilatation usually signifies the side of the hematoma. However, in the series of cases on which we have based this communication pupillary dilatation could not be considered an important sign. Possibly in some instances transient dilatation was overlooked. The pupil was dilated and fixed or sluggish in its reaction to light on the side of the lesion in 5 adult patients, and in 1 patient the pupillary change was contralateral to the lesion. These figures are small as compared with those of Kennedy and Wortis¹⁰ who found in a series of 72 cases of subdural hematoma homolateral

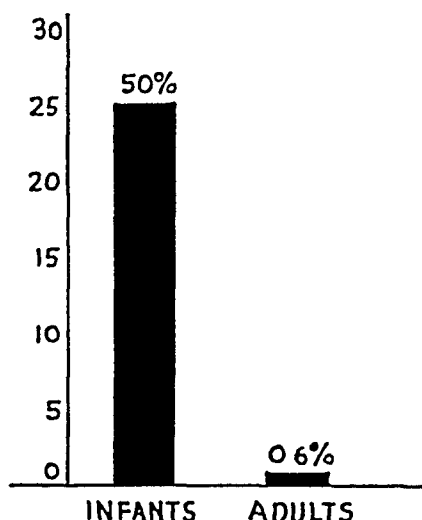


Fig 6—Incidence of retinal hemorrhages in infants and in adults with subdural hematoma

dilatation of the pupil in 30 and contralateral dilatation in 12. Kunkel and Dandy gave this sign little consideration in their study. In 1 adult with bilateral subdural hematoma we observed unilateral pupillary dilatation.

There is general agreement, and we have observed, that dilatation of the pupil disappears certainly within a few hours, and sometimes within a few minutes, after evacuation of the hematoma.

It is only recently that we have had an explanation for homolateral dilatation and fixity of the pupil in cases of subdural hematoma and of

9 Woodhall, B., Devine, J. W., Jr., and Hart, D. Homolateral Dilatation of Pupil, Homolateral Paresis and Bilateral Muscular Rigidity in Diagnosis of Extradural Hemorrhage, *Surg, Gynec & Obst* **72** 391-398, 1941.

10 Kennedy, F., and Wortis, H. Acute Subdural Hematoma and Acute Epidural Hemorrhage, *Surg, Gynec & Obst* **63** 732-742, 1936.

subarachnoid and extradural hemorrhage Reid and Cone¹¹ and Woodhall and associates, among others, described herniation of the hippocampus or the medial aspect of the temporal lobe and midbrain through the tentorium. As a result of such herniation, there is pressure on the homolateral third nerve, with the development of an internal ophthalmoplegia, which may be associated with ptosis. Reid and Cone demonstrated such herniation in experimental animals and found that homolateral pupillary dilatation developed. In their animals there were no hemorrhages in the midbrain, but in some instances hemorrhages developed in the occipital lobes. Although absence of hemorrhages in the midbrain suggests that involvement of the nucleus of the third nerve is not responsible for the pupillary dilatation, the experimental work of Magoun and associates¹² is even more convincing in this regard. These observers found that stimulation of the gray matter in the region of the nucleus invariably produced bilateral pupillary constriction, whereas stimulation of the peripheral nerve invariably produced homolateral pupillary narrowing. Ecker and Anthony¹³ suggested that traction of the third nerve on the sphenoid bone, rather than pressure on the nerve, may be the cause of the pupillary change. Although there can be no reasonable doubt that herniation occurs, as has been described, and that it is associated with the pupillary change, the actual mechanism is not completely understood. The pupillary pathways are known to be peripheral in the nerve. While this explains the internal ophthalmoplegia, it is difficult to understand why a more complete paralysis of the third nerve does not occur frequently. We have never observed total paralysis of the third nerve in a case of subdural hematoma but have observed such a paralysis frequently as a result of aneurysm, and in both instances pressure on the third nerve seemed to be the etiologic factor.

Both in infants and in adults our series contained cases of bilaterally dilated and fixed pupils. Possibly hemorrhages in the midbrain were present in these cases. Also, we observed bilateral narrowing of the pupils, which seemingly was an expression of an irritative miosis.

Exophthalmos—We observed bilateral proptosis in 1 infant not included in this series, but there was free blood in the orbital cavity.

Ptosis—Ptosis may or may not be present on the side of pupillary dilatation. Unilateral ptosis was present in 6 patients, and in 5 it was

11 Reid, W. L., and Cone, W. V. The Mechanism of Fixed Dilatation of the Pupil Resulting from Ipsilateral Cerebral Compression, *J. A. M. A.* **112** 2030-2034 (May 20) 1939.

12 Magoun, H. W., Atlas, D., Hare, W. K., and Ranson, S. W. The Afferent Path of the Pupillary Light Reflex in the Monkey, *Brain* **59** 234-239, 1936.

13 Ecker, A. D., and Anthony, E. W. Head Injuries from the Ophthalmologist's Viewpoint, *Brit. J. Ophth.* **29** 43-48, 1945.

on the side opposite the subdural hematoma. Possibly such a contralateral ptosis is supranuclear in origin, although, theoretically, abolition of cortical impulses might result in increased tone in the levator muscle. We have not seen cases in which a diagnosis of supranuclear ptosis could be made with certainty. Pronounced bilateral ptosis was present in a single case.

Involvement of the Third Nerve—We have not seen an instance of total paralysis of the third nerve. Furthermore, we observed ptosis in association with homolateral pupillary dilatation in only 3 patients.

Involvement of the Sixth Nerve—Of our adult patients, there was unilateral paresis of the sixth nerve in 3 and bilateral paralysis in 1.

Nystagmus—This sign was mentioned frequently in the case reports of infants. It may have originated in defective ocular fixation. It was present in only 3 adults. Probably the ocular movements of nystagmus in adults are dependent on palsies of conjugate movements.

Conjugate Deviation of the Eyes—In 2 adults the eyes were deviated away from the side of the lesion. Since this deviation was persistent, it seemed unlikely that it resulted from an irritative lesion, rather, it appeared to be due to an interruption to the supranuclear pathways in the hemisphere opposite the side of the lesion. Conjugate deviation of the eyes was seen frequently in infants as part of convulsive episodes when they did not have recognizable localizing value.

Visual Field Defects—These were noted in a minority of the patients. Maltby¹⁴ found evidence of a visual field defect in only 7 of 62 cases (11 per cent). The field defects were homonymous and contralateral to the side of the clot in 5 cases, ipsilateral in 1 case and left sided in a case in which the clot was centrally situated. Maltby expressed the belief that the field defects were due to obstruction of circulation through branches of the posterior cerebral artery as the result of herniation of the temporal lobe through the tentorium. He stated that the field changes had more lateralizing value than the pupillary anomalies already described. We observed homonymous hemianopsia for colors in only 1 patient and contralateral hemianopsia in another.

Also, we observed total blindness and total atrophy of the optic nerve in 2 patients. One patient, a youth 18 years of age, was moribund when he was brought to the hospital, his visual acuity was said to have been very defective, after operation it remained at bare perception of light and was unchanged three years later. The other patient was a man who had been operated on elsewhere, he was completely blind at the time of our examination, but he stated that his vision had been tolerably good before his operation.

14 Maltby, G. L. Visual Field Changes and Subdural Hematomas, Surg., Gynec. & Obst. **74** 496-498, 1942.

Loss of Corneal Reflex—This has been described as occurring on the side of the lesion. We do not have accurate information regarding it in cases of subdural hematoma.

AN OBSERVATION CONCERNING PATHOGENESIS

In compiling this report, we were attracted by the rarity of subdural hematoma in the age group from 2 to 20 years, the regularity with which the hemorrhage occurred bilaterally in infants and unilaterally in adults, the regularity with which blood (or xanthochromia) was found in the spinal fluid of infants and its almost uniform absence in adults, and the frequent absence of a history of trauma in infants and the almost invariable history of trauma in the adults.

In an attempt to explain these differences, several infant and adult brains were examined. Gross examination revealed an important anatomic difference between the supporting structures of the pial veins of the infant and those of the adult. These differences, although recognized by anatomists, have never been associated with the pathogenesis of subdural hemorrhage.

To demonstrate these differences, it is necessary to divide the dura a few centimeters from the midline of the convexity. In the infant the dura and the delicate arachnoid membrane are easily separated, and when the dura is retracted toward the midline several large pial veins are seen entering the longitudinal sinus. These vessels are short, non-tortuous and without support. Grossly, they appear to lie free in the subdural space for distances varying from a few millimeters to 1 cm before entering the longitudinal sinus. The veins do not pass directly from their location in the pia into the sinus but follow a diagonal path and enter the sinus at an angle.

In sharp contrast to the condition seen in the infant, the dura and the arachnoid membrane of the adult are firmly bound together in the region of the longitudinal sinus. This attachment of the arachnoid to the dura is formed by masses of fibrous tissue, forming the base of arachnoid villi (pacchionian granulations). These differences are apparent in the drawings made from a specimen of brain from a normal infant and one from an adult.

These fibrous attachments were described by Weed¹⁵ as representing fully developed arachnoid villi. The invasion of the dura by the delicate arachnoid villi occurs in infancy. In infants they are microscopic, offer little support and are not visible. Our observations indicate that these structures become visible soon after the period of infancy. The villi observed in 4 and 5 year old children were comparable in development to those of an adult.

¹⁵ Weed, L. H. Studies on Cerebrospinal Fluid, J. M. Research 26 51-113, 1914-1915.

The effect of these anatomic differences on the movement of the brain within the cranial cavity is not known. One would think, however, that the movement should be much freer in the infant than in the adult, for the attachment of the arachnoid to the dura in the adult brain ought necessarily to limit its movement. It would seem likely, also, that in the infant when the pial vessels entering the longitudinal sinus

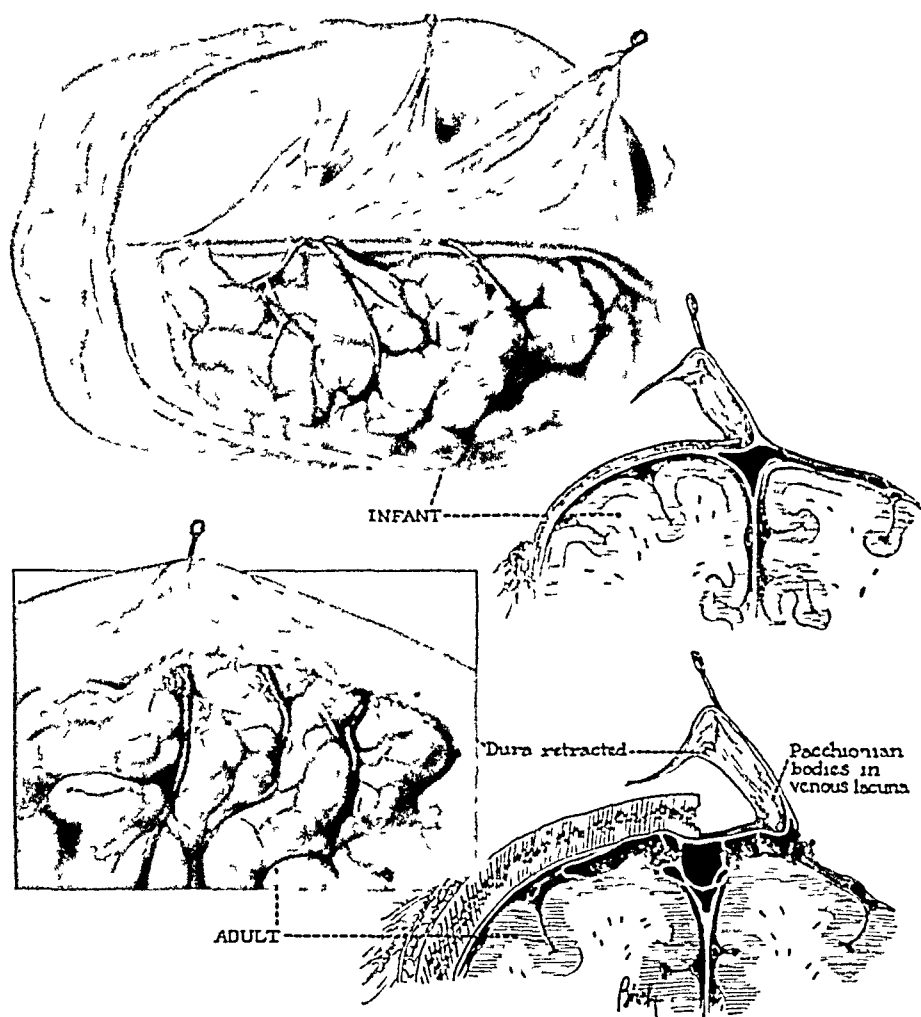


Fig 7—Differences in the relation of the dura and the arachnoid membrane in the region of the longitudinal sinus in the infant and in the adult

rupture the arachnoid would be torn simultaneously and the blood would find its way into the subarachnoid space as well as between the outer surface of the arachnoid and the dura. It is plausible to think that in the adult, on account of the presence of these fibrous attachments, which must protect the pial veins entering the longitudinal sinus, a severer trauma would be required to rupture the vessels. The usual absence of a history of trauma in infants may perhaps be explained on the

ground that only slight trauma might be required to rupture the veins in the infant on account of the freer mobility of the brain. The freer mobility of the brain might also explain why the subdural hematoma in the infant is almost invariably bilateral.

Differences in the anatomic arrangements of the membranes of the brain in the infant and in the adult require further studies.

Wilmer Ophthalmological Institute

DISCUSSION

DR J PARSONS SCHAEFFER, Philadelphia. I should like to know how many of the subdural hematomas at the early ages mentioned were the result of birth injuries. My other point has to do with the variation in size of the optic foramen through which the optic nerve passes into the orbit. When the opening is roomy, it might be inferred that the subdural hemorrhage would readily pass into the dural-arachnoid interspace and that failure of blood to do so might be due to the bony encroachment on the optic nerve and its sheath and interspaces.

DR FRANCIS HEED ADLER, Philadelphia. The high incidence of subdural hematoma in infants could be logically explained by the prevalence of birth injuries. Every normal birth exposes the child to cranial compression, and since the fontanelles are open then and for some time after birth, it is no wonder that there should be a high incidence of intracranial trauma. From the time that the fontanelles close, the child is not often exposed to any serious intracranial damage until he reaches the age at which serious accidents are apt to occur. In other words, the falls and bumps of the nursery do not produce intracranial lesions, but industrial accidents often do. It would seem much more logical to assume that this explains the distribution of subdural hematomas according to age than to base this incidence on an anatomic difference in the cranial contents in the infant and in the adult.

Dr Walsh has asked me to comment on ptosis as a sign of supranuclear paralysis. Since the muscles of the lid have a separate representation in the frontal cortex, it is possible to have a supranuclear paralysis with a lesion situated anywhere from the cortex down to the nucleus. This, of course, is not true of the individual muscles controlling the movements of the eyeball. Furthermore, the fiber tracts for the levator and muscles (the latter is questionable) run together with the fiber tracts for upward and downward movements of the eyeballs in the region of the corpora quadrigemina. Accordingly, lesions in this region cause disturbances of upward and downward movements of the eyes, together with ptosis and tucked lids. A few years ago Collier called attention to ptosis and retraction of the lid as signs of supranuclear paralysis of the third nerve, differentiating these lesions thereby from lesions affecting the third nerve itself or the nucleus. If the lesion is anterior, retraction of the lid is likely to be present, whereas if the lesion is posterior ptosis occurs.

DR WALTER I LILLIE, Philadelphia. Dr Walsh is to be congratulated on his presentation of a difficult subject as the classification of traumatic cerebral changes is not always well differentiated. Clin-

ically, it is often difficult to correlate the multiple, bizarre changes with a single lesion. Although a single large lesion is present, associated small multiple lesions help to explain the syndrome. Dr. Walsh has not explained specifically why a subhyaloid hemorrhage occurs in infants and not in adults. The occurrence of subhyaloid hemorrhages in adults is usually associated with a compression injury to the chest or the neck, but that it may occur from intracranial venous compression is a possibility.

The diagnosis of subdural hematoma is usually supported by an encephalogram, as the variations in the fluid channels reveal the space-taking lesion.

The occurrence of general convulsions in adults should suggest a lesion of the frontal, temporal or occipital lobe. Such patients should have a routine perimetric examination of the fields, as a quadrantal homonymous hemianopsia has often been found a year or two in advance of other definite signs of a space-taking lesion.

DR. HENRY A. SHENKIN, Philadelphia. I should like to comment from the neurosurgeon's point of view. Dr. Walsh made an effort to distinguish between the symptoms of subdural hematoma in the child and those in the adult, and it is true they are quite different. The fact that there are open fontanels in the infant would well account for the difference in symptoms.

In adults papilledema does occur, but my experience is that it rarely is seen in infants. The open fontanels could permit sufficient expansion of the calvaria to absorb the pressure. The presence of convulsions in childhood may well be due to a lowered convulsive threshold, said to be characteristic of infancy. However, the length of time to which the cortex is subjected to irritation may be the convulsive factor. It is known that cerebral tumors of slow growth are the ones most frequently associated with seizures, and, by analogy, subdural hematoma of long duration may be more frequently associated with seizures. The open fontanels, compensating for the increased mass of the hematoma, permit the child to survive for periods far in excess of the usual period in which the life of an adult would be threatened by a chronic subdural hematoma. It is likely that the subdural hematoma of infancy is caused by trauma at birth. The appearance of the lesion and the history of the child's development substantiate this. The neurosurgeon is usually consulted when the child is 6 to 12 months of age. On the other hand, adults usually manifest life-threatening symptoms from chronic subdural hematoma six to twelve weeks after their injury.

Unilateral dilatation of the pupil is more characteristic of acute subdural hematoma than of the chronic form. I believe subdural hematoma of infancy is more nearly analogous to the latter entity than to the former. Indeed, ipsilateral dilatation of the pupil is far more characteristic of the fulminating syndrome of acute epidural hemorrhage than of the more slowly developing acute subdural hemorrhage.

I agree that the results of treatment of subdural hematoma of infancy are poor. I think that this can be explained by the delay in making a proper diagnosis. The growing brain is compressed for undue periods, and often it never recovers sufficiently to develop to its full capacity.

DR J PARSONS SCHAEFFER, Philadelphia I should like to pose a question There is some thought that the facial nerve may, in some manner, be responsible for the peculiar behavior of the upper eyelid in certain cases Some of the fibers that arise from the nucleus of the oculomotor nerve descend in the medial longitudinal fasciculus and either terminate about the cells of the nucleus of the facial nerve or join the facial nerve as such, passing in this nerve to the upper part of the orbicularis oculi muscle, thus associating the innervation of the levator palpebrae muscle with that of the orbicularis oculi muscle Although it is generally accepted that the oculomotor nerve supplies the levator palpebrae muscle and that the orbicularis oculi muscle is supplied by the facial nerve, this intermingling of the fibers of the two nerves may well be variable enough to account for such peculiar manifestations with reference to the action of the upper eyelid Much more study is needed

The other point concerns the newborn infant, to whom Dr Walsh referred There is no doubt that the veins as they course to enter the superior sagittal sinus are fairly free, but it is equally true that there is a mesothelium covering them that does not add much protection Later, in the adult, as the cerebral membranes become more pronounced and the interspaces are developed, the parts become matted together near the superior sagittal sinus Also, the arachnoid and the subarachnoid spaces, in the form of arachnoidal granulations, protrude into the superior sagittal sinus, the endothelium of course being crowded ahead This adds to further crowding near the venous sinus and encroachment on the cerebral veins as they enter the dural sinus

DR FRANK B WALSH, Baltimore In reply to Dr Schaeffer, I may say that in some infants birth injury is a possible explanation for subdural hematoma It is extremely doubtful whether it was operative in a majority of our infants We have not made studies on the optic foramina

Except for some of the literature concerning the joint innervation by the third, seventh and ninth nerves, I confess to knowing nothing However, I am flattered to have been asked this question by Dr Schaeffer, despite my inability to answer it

Dr Adler's explanation of supranuclear ptosis involving the lid opposite the hematoma is interesting However, there is no characteristic feature in such a ptosis that would eliminate the possibility of its having been produced by a homolateral incomplete palsy of the third nerve I was glad attention was drawn to Collier's paper, which I recommend as excellent

I agree with Dr Lillie that in these cases there may be multiple lesions I am unable to explain preretinal hemorrhages seen in cases of subarachnoid hemorrhage It is thought that such retinal hemorrhages are venous in origin One would think they might be associated with sudden increase in intracranial pressure However, Gardner has shown that the intracranial pressure in many cases is not increased

CHOROIDEREMIA

Report of a Case

BENJAMIN ESTERMAN, M D

NEW YORK

THE TERM choroideremia has been used to describe an apparent absence ophthalmoscopically of the entire choroid except in the macular region. Since the first description, in 1872 by Mauthner,¹ 31 cases of a condition described as choroideremia have been published in the literature. These were cited by Nettleship,² Wolf³ and Parker and Fraclick.⁴ In 1937 Bedell⁵ gave an excellent summary of each of the then published cases which he considered instances of choroideremia in the broader sense, the description of these cases does not need to be repeated here. He added 5 cases of his own. Six years earlier, in a discussion on Parker and Fraclick's paper, he suggested that choroideremia may appear in more than one form. Since that time Friedman⁶ (1940), Scobee⁷ (1943), Shapira and Sitney⁸ (1943) and Magder⁹ (1945) have reported cases.

Friedman's⁶ case was that of a man of 45 who had always experienced night blindness and who stated that one uncle had a similar condition. He had myopia of about 6½ D with corrected vision of 20/30 + in the right eye and 20/50 — in the left eye and concentric contraction of the fields to about 10 or 15 degrees. The disks were normal, as was the retinal circulation. The choroid was absent except for that in the macular regions, some remaining choroidal vessels and a few clumps of pigment.

From the Manhattan Eye, Ear and Throat Hospital, service of Dr R Townley Paton

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Jan 21, 1946. A discussion of this paper was published in the August 1946 issue of the ARCHIVES, page 245.

1 Mauthner, L. *Ber d naturw-med Ver in Innsbruck* **2** 191, 1871

2 Nettleship, E. *Roy London Ophth Hosp Rep* **17** 373, 1907-1908

3 Wolf, S. *Choroideremia*, *Arch Ophth* **3** 80 (Jan) 1930

4 Parker, W R, and Fraclick, F B. *Choroideremia. Report of a Case*, *Arch Ophth* **6** 213 (Aug) 1931

5 Bedell, A J. *Choroideremia*, *Arch Ophth* **17** 444 (March) 1937

6 Friedman, B. *Choroideremia*, *Arch Ophth* **23** 1285 (June) 1940

7 Scobee, R G. *Am J Ophth* **26** 1135, 1943

8 Shapira, T M, and Sitney, J A. *Am J Ophth* **26** 182, 1943

9 Magder, H. *Choroideremia. Report of a Case*, *Arch Ophth* **33** 468 (June) 1945

Scobee⁷ reported 2 cases of the condition in brothers, the disease in the older, aged 24, being in an advanced stage, and that in the younger, aged 18, in an early stage. The absence of symptoms in the childhood history of the patient with the more advanced disease, together with the apparent worsening of the subjective and objective findings during the month in which both patients were under observation, led Scobee to agree with Bedell that the condition is not congenital but acquired. The presence of evident degenerative changes in the vitreous (pigment balls, striation of fibrils in the anterior portion of the vitreous) tended further to point to the acquired nature of the disease in these cases.

Shapira and Sitney's case, the second in which the disease had been reported in a female, was that of a woman aged 52 with hypertension and syphilis of the central nervous system. Argyll Robertson pupils, corneal scarring, pigment, posterior corneal deposits, aqueous flare and posterior synechias. The condition was seen by a number of observers, who pronounced it choroideremia, even in the light of Verhoeff's caution regarding confusion with retinal gliosis.

Magder's case was that of a man aged 58 with no family or personal history of ocular disorder except for night blindness, which had always existed but had become worse during the last ten years. He had low myopia, correctible to 20/20 and 20/30, with fields contracted to within 10 degrees of fixation plus a narrow crescentic peripheral area. The choroid was absent in each eye except for the macular region and the extreme periphery. A few remaining choroidal vessels were seen, as were several clumps of pigment.

The condition is always bilateral, occurs almost invariably in males, is usually associated with night blindness and sharply contracted visual fields, but often with relatively unimpaired central vision, and in the majority of instances occurs in persons with myopia of moderate degree. The history of defective vision and visual fields is usually of long standing going back as far as the patient can remember in most cases, and the process has often remained stationary during the life of the patient. A few cases have been reported in brothers, but in no instance has there been consanguinity in the parents, nor has any authentic case been found of the existence of the same condition in a parent or a grandparent or in offspring.

REPORT OF A CASE

D. H., a white man aged 29, was admitted to the eye clinic of the Manhattan Eye, Ear and Throat Hospital, service of Dr. R. Townley Paton on March 6, 1945. His chief complaint was night blindness, which had always been present but which he claimed had increased somewhat in the past few years. Dark adaptation had always been difficult, and distant vision had always been poor without glasses. With glasses his central vision had been such as to enable him to do clerical work. Central color vision was not impaired.

The family history was negative for consanguinity and was otherwise irrelevant except that two uncles were said to have had poor vision, the nature and cause of which were unknown. No evidence could be obtained pointing to syphilis in the past history of the patient or of his family, there was no recollection of ocular or cranial injury or of any ocular inflammatory disease.

The physical examination revealed an entirely normal condition as did dental and rhinologic examinations, roentgenologic studies of the chest, urinalysis, the Wassermann test, the Mantoux test and hematologic studies.

Visual acuity was 5/200 in the right eye, improved to 20/200 with —6 D sph —2 D cyl, axis 180, and 10/200 in the left eye, improved to 20/30 with —4.50 D sph —1.25 D cyl, axis 180. The visual fields were found to be reduced to within 5 degrees of fixation in each eye, using a 10 mm white stimulus at 330 mm.

The lids, lacrimal apparatus, conjunctivas and corneas were normal, the anterior chambers were of normal depth, the irises were normal, the pupils reacted properly both directly and consensually to light and in accommodation and dilated readily with mydriatics to disclose a clear lens and vitreous. Transillumination was similar to that seen in albinotic eyes. Intraocular tension was soft. All extraocular movements were unimpaired.

Ophthalmoscopic Examination—Right eye. The disk was of good color with sharp margin and a small physiologic excavation, the lamina cribrosa was not seen. The retinal arteries and veins were of normal caliber and distribution. A pyriform area 3 by $1\frac{1}{2}$ disk diameters in the macular region and a small pink spot between this and the disk were all that remained of the choroid, the rest of the fundus appearing as a faintly stippled white, with a few scattered pigmented areas, as shown in figure 1, and one rather dense area lying in the macular region, and possibly accounting for the fact that central acuity in the right eye could not be improved beyond 20/200. Passing just behind this patch of pigment was a group of five choroidal vessels, which had perforated the sclera, branched and fanned out temporarily to fade away after running behind an ascending branch of the inferior temporal vein. A few other branches of the posterior ciliary vessels were seen perforating the sclera, superior and nasal to the macular region, while two entered the globe about 3 disk diameters temporal to the macula, passed behind a clump of pigment and faded away as they coursed peripherally.

Left Eye. The disk was of good color, but there was a faint blurring of the margins, only a suggestion of a physiologic excavation was evident and no lamina cribrosa was visible. The retinal vessels were normal. A round area, 3 by 3 disk diameters, in the macular region, a small T-shaped area superior and temporal to the disk and a faint spot in the temporal periphery were the sole remnants of the choroid in this eye. The rest of the fundus was a faintly stippled white with a few pigment areas, one of which plainly lay behind a branch of the superior temporal artery and vein. Emanating from the macular regions were a few choroidal vessels, most of which coursed temporally for a short distance and disappeared, while one traveled nasally and upward to lose itself behind a branch of the superior temporal vein. A somewhat unusual feature was the striking difference in macular vision in the two eyes. In spite of the fact that in each eye the choriocapillaris and the pigment epithelium of the macular area were spared, there was ophthalmoscopic evidence of macular degeneration in the right eye. This was probably quite independent of the choroideremia, since it is conceivable that an eye which has more than 6 D of myopia may show macular changes in its own right.

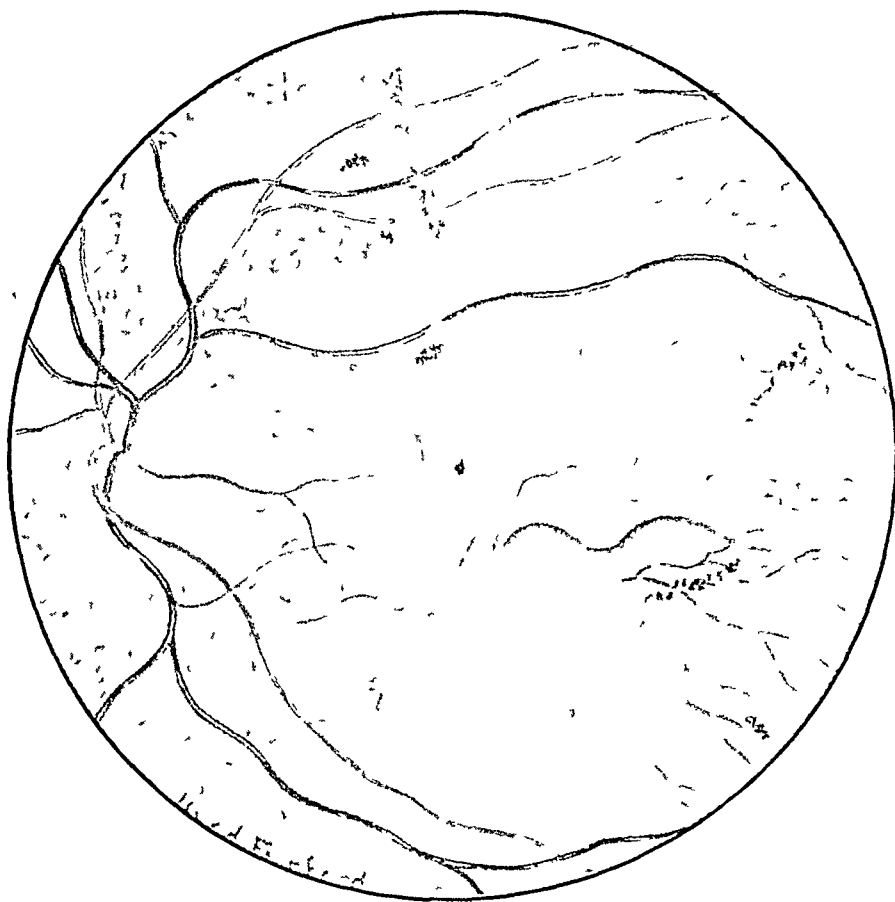


Fig 2—Choroideremia, left eye

COMMENT

The knowledge of the nature and etiology of choroideremia is largely speculative owing to the absence of histologic data. Mann¹⁰ expressed the belief that the defect is due to failure of the posterior ciliary arteries to develop or is associated with failure of the outer layer of the optic cup to produce pigment. She stated

The choroidal net seems to develop wherever mesoderm is in contact with pigment epithelium. It appears with the pigment and seems to be in some way related to this, in that if for any reason pigment is absent over an area of the surface of the optic cup, the choroid is absent also.

She cited the instance of a certain area below the optic nerve in birds which is normally unpigmented and over which choroid does not develop. Collins and Mayou attributed the condition to failure in the formation of blood vessels in the inner part of the mesoblast except for the vessels supplying the macula.

In explanation of the sparing of the macular region, Connor¹¹ said.

The analog in embryonic life of what is later the macular area of the fundus is a spot in the outer surface of the secondary optic vesicle where the first signs of differentiation of the mesoblast into sclera and choroid are seen, the first appearance of the choroid being manifest by a tiny plexus of capillaries at this point. Hence, in seeking an explanation of the cause of choroideremia, we must consider that differentiation of the mesoblast of the secondary optic vesicles into sclera and choroid began in a normal way and at the normal point, but for some reason was arrested when only the macular region was supplied with choroid.

Nettleship explained the appearance of patches of pigment by the fact "that the retinal epithelium is laid down in the first few weeks of embryonic life before the choroid which is to nourish it has been differentiated, therefore, if the choroid atrophies or does not develop, we should expect that the epithelial pigment, so far as it has been formed, would retrogress and migrate."

DIFFERENTIAL DIAGNOSIS

Choroideremia must be distinguished principally from retinitis pigmentosa, gyrate atrophy, choroidal sclerosis and massive retinal gliosis.

Uncomplicated retinitis pigmentosa is easily differentiated by the presence of many bone-corporuscle-like deposits of pigment, the waxy pallor of the disks and the marked attenuation of the retinal vessels, all of which are absent in choroideremia.

The gyrate atrophy of Fuchs and Cutler characteristically begins in the periphery with numerous irregular areas of choroidal atrophy, separated by normal-appearing fundus. These areas grow larger and often

10 Mann, I. *The Development of the Human Eye*, New York, The Macmillan Company, 1928, *Developmental Anomalies of the Eye*, *ibid*, 1937.

11 Connor, A. B. *Am J Ophth* 2:553, 1919.

coalesce, while concomitant atrophy develops in the area adjacent to the nerve head. It is only the final picture which might be confused with that of choroideremia, but, unlike the latter, the history is that of extremely slow progress over a great many years.

Choroidal sclerosis is a degenerative vascular disturbance of the choroid primarily, and of Bruch's membrane, the pigment epithelium and the retina secondarily. This condition is more commonly found in elderly persons with evidence of vascular changes elsewhere in the body, and the sclerotic process in the larger choroidal vessels can be seen ophthalmoscopically, especially since these are frequently set off against pigment, which has migrated into the intervascular spaces. Some of this pigment migrates into the layers of the retina as well, often lying anterior to the retinal vessels. Colloid bodies or drusen, may appear on Bruch's membrane as an expression of degenerative changes of that structure. The disk is frequently pale and wax, while central visual acuity, the visual field and light sense deteriorate progressively and to a marked degree.

Massive Gliosis. Verhoeff¹² implied that the diagnosis of true choroideremia depends on the complete absence of choroid except for the macular region, the absence of pigment and an absolutely white sclera visible throughout the fundus. He claimed that many so-called cases are in fact cases of retinitis pigmentosa with choroid intact but hidden from view by widespread, deep-seated retinal gliosis. By way of illustration, he mentioned 5 cases of retinitis pigmentosa in one family, in 2 of which (both of males) the fundi closely resembled the classic conception of choroideremia, and he suggested that widespread gliosis accompanying retinitis pigmentosa is a male characteristic.

Careful study of the fundi in the present case, as well as of the paintings in the papers of Parker and Frazer and of Benjamin Friedman, leads me to doubt greatly that gliosis in these cases could have been so widespread and massive as to produce fundi of such pallor and yet fail to obscure those few choroidal vessels outside the macular region. In all three papers choroidal vessels may be seen as they perforate the sclera, testifying to their depth in the choroid. Surely, gliosis sufficient to obscure the more superficial choriocapillaris and pigment epithelium should have hidden these deeper vessels as well. I would suggest this point as a criterion for differentiating massive gliosis and choroideremia.

SUMMARY

A case of choroideremia is presented in a white man aged 29 with moderate myopia and some macular degenerative changes in one eye with

12 Verhoeff, F. H. Retinitis Pigmentosa with Widespread Gliosis. So-Called Choroideremia, *Arch. Ophth.* 27: 688 (April) 1942.

resultant acuity of 20/200, while vision in the opposite eye was correctible to 20/30. The salient points of typical choroideremia are outlined, and the more recent cases in the literature (published since Bedell's review, in 1937) are briefly summarized. In the absence of histologic data, some of the published speculations regarding the cause and nature of the disease are reviewed. Finally, a brief differential diagnosis of choroideremia, retinitis pigmentosa, gyrate atrophy, choroidal sclerosis and massive gliosis is presented.

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MYOPIA INVERSA

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Translated from the German by Erich Pressburger, M D, San Francisco

A CONUS inferior, which is spoken of in English-speaking countries as the Fuchs coloboma, after my father, is located below and either to the temporal or to the nasal side of the disk. It sometimes has a horizontal¹ or a somewhat oblique straight line at the edge of the disk and is characterized by the fact that the lower half of the fundus usually has less pigmentation than the upper half. The error of refraction of the lower half of the fundus is also frequently greater than that of the upper. Myopia is found in a majority of the cases. In histologic sections, a thinning of the sclera has been noted in the lower quadrants.²

A nasal conus³ occurs less frequently than the inferior conus and often shows a lesser degree of pigmentation of the fundus on the nasal side and occasionally a bulging of the sclera, which can be determined by the difference in refraction of this area. In the cases of nasal conus the fovea frequently lies closer to the disk than normally. While the blindspot is situated in the normal position with respect to the fixation point, my father was able to observe in 2 cases on histologic examination that there was a considerably shorter distance between the margin of the disk and the fovea.⁴ There is nearly always an inverse type of arrangement of vessels in the cases of nasal conus, and in these cases a medium or a great degree of myopia is apt to be present. The following cases indicate that myopia has a special connection with the nasal conus.

CASE 1—A woman aged 51 had a large nasal conus in the right eye adjoining a round disk, without any inverse type of vessel arrangement, and a myopia of 15 D, while in the left eye there was a normal fundus with normal refraction.

CASE 2—A man aged 54 had a nasal conus and a myopia of 10 D in his right eye, while in the left eye he had an inferior and a nasal conus and a myopia of 7 D.

1 Fuchs, E. *Lehrbuch der Augenheilkunde*, ed 17, Vienna, F. Deuticke, 1944, illus 10, pl 1.

2 Fuchs, A. *Die Erkrankungen des Augenhintergrundes*, Vienna, F. Deuticke, 1943, illus 1, pl 4.

3 Fuchs,² illus 4, pl 1.

4 Fuchs, E. *Klin Monatsbl f Augenh* 62 433, 1919.

As Roenne⁵ has demonstrated, in cases of nasal conus the nasal parts of the fundus show a greater degree of myopia than the macular region or the temporal fundus

There are occasional cases in which changes occur at the disk which resemble the nasal conus but which are something quite different. They have not attracted much attention until now, but they are entitled to special notice. In these cases, on the nasal side of the optic nerve one finds changes which look exactly like those on the temporal side of the optic nerve in cases of high myopia, namely, large atrophic zones of the choroid (circumpapillary atrophy), which extend toward the nasal side more than toward the temporal side. As such eyes are myopic, I propose to call these changes "myopia inversa." In the course of twenty years, I have made notes on 14 such cases and have drawn schematic sketches of the fundi.

CASE 1—A woman aged 75 had vision of 6/18 in the right eye with a —4 D lens. The disk showed an inverse type of vessel arrangement, and at the nasal margin of the disk there was a sharply defined zone, measuring 3 by 1½ papilla diameters (p d.). This zone was white and somewhat yellowish in parts, partly dotted and more extensive in the upper than in the lower region (fig 1). There were no changes in the vessels in this region. Below the disk there was a blurred, reddish area, ¾ p d. in size, next to the margin of the disk. The nasal half of the fundus had a lighter pigmentation and appeared albinotic, while temporal to the disk the fundus was tessellated. Retinoscopic examination could not be performed because of heavy opacities in the vitreous. The fovea seemed to lie closer to the margin of the disk than normally. The blindspot was enlarged at the top and even more so at the bottom. There was no change in its position, however. The left eye showed a myopia of 15 D and had a wider zone of atrophy of the pigment epithelium at the nasal side of the disk, but not so broad as one as the zone in the right eye. An inverse type of vessel arrangement was also present. In both eyes this disk looked perfectly round.

CASE 2—A 14 year old boy when seen in December 1925 had a refraction of —3.5 D sph —1.25 D cyl, axis 20 in the right eye. The disk showed an inverse type of vessel arrangement and was somewhat oval. At the nasal margin of the disk there was a half-moon-shaped area of atrophy of the pigment epithelium. The pigmentation of the fundus was not as pronounced nasally as temporally. The fovea seemed to be normally distant from the disk. In the left eye, there was a refraction of —3.00 D sph —2.5 D cyl, axis 10. The left disk showed only an inverse type of vessel arrangement and had a long, vertical oval form, but here again the nasal fundus was less pigmented than the temporal. In 1943 I was able to examine this patient again, after an operation had been performed elsewhere for divergent strabismus. The operation was not entirely successful, as he still had a divergence of 20 degrees. The patient at this time was 32 years of age. The refraction in his right eye was —8.00 D sph —1.00 D cyl, axis 15. Thirty degrees nasal to the fovea, the refraction was —15.00 D sph —1.00 D cyl, axis 25. The atrophic zone had become larger and surrounded the disk. Nasally, this zone was 1½ p d. wide, while on the temporal

5 Roenne Klin Monatsbl f Augenh 57 512, 1916

side it was extremely narrow (fig 2). Above the fovea, a small, white atrophic spot had developed. A similar white spot lay nasal to the disk and had an irregular pigmentation, like a small pigment dot, which also showed up in the yellowish atrophic zone. The left eye had a refraction of -2.5 D sph $\ominus -2.00$ D cyl, axis 15. Thirty degrees nasally from this fovea, the refraction was -10.00 D sph $\ominus -3.00$ D cyl, axis 177. The disk showed the same vertical oval formation, with an inverse type of vessel arrangement, as previously mentioned. In both eyes, the lack of pigment in the nasal fundus was very conspicuous. The fovea seemed to be at a normal distance from the disk. This was the only case in which I had an opportunity to make examination after a long interval. I noted a definite increase of the myopia in the right eye, with a nasal atrophic zone, and this had become appreciably larger. When I saw the zone on the patient's fourteenth birthday, I noted on the nasal side only a white, half-moon-shaped area, but in his thirty-second year circumpapillary atrophy had developed. In addition, a pigment spot had formed in the atrophic section, and other atrophic spots could be discerned in the fundus. From the fact that this eye alone disclosed a considerable increase of myopia, while the other, with a negligible increase in the refraction, showed no change in the disk one might deduce that there was a real connection between the atrophic zone and the myopia, evidently, the atrophic zone was already considerably developed at a time when the myopia of the posterior pole was insignificant. Two points were interesting. First, the patient had a divergent squint of the left eye; this eye had no particular myopia and had become amblyopic. His vision of 6/8 in 1925 dropped to perception of hand movements without any changes in the fovea. One would have expected just the opposite, namely, that he would be amblyopic and would squint with the right eye, this eye being myopic and showing pronounced changes in the fundus. Second, in spite of the marked difference in the refraction of the posterior pole, there existed a considerable degree of myopia of the nasal fundus, as a result of the bulging of the nasal sclera in both eyes. On retinoscopic examination, it was obvious that in the left eye a much higher degree of astigmatism appeared in abduction than when the patient looked straight ahead. In the right eye I found the same astigmatism in the two positions, namely, in abduction and when the patient looked straight ahead. In the left eye, however, not only did I find an increase of from 2 to 3 D in cylinder, which might have been due to marginal astigmatism, but I also observed that the axis was 15 degrees and the axis of the nasal fundus was 177 degrees. This striking discrepancy of the axes was probably due to the torsion of the eye when turned to the side.

CASE 3—A man aged 56 had a refraction of -2.25 D sph $\ominus -1.00$ D cyl axis 180 in the right eye, an inverse type of vessel arrangement, an oval and oblique disk and a large conus on the temporal side and below. He also had arteriosclerotic retinopathy with occasional white spots and hemorrhages (fig 3). In the left eye I found his refraction to be -3.00 D sph $\ominus -2.50$ D cyl, axis 10, here, too, the disk was oval but in a vertical position. The distribution of the vessels was inverse, and nasally there was an adjacent atrophic zone about 2 p d wide and $2\frac{1}{4}$ p d high. At the same time, three fourths of the disk was surrounded by the atrophic zone. Several retinitic spots were also found, with no marked difference in the pigmentation between the nasal and the temporal fundus.

CASE 4—A woman aged 63 complained that objects were distorted with her right eye. Vision in the right eye was 6/60 with a correction of -4.00 D sph $\ominus -1.00$ D cyl, axis 180 and 6/60 in the left eye with a -4.00 D lens. In both

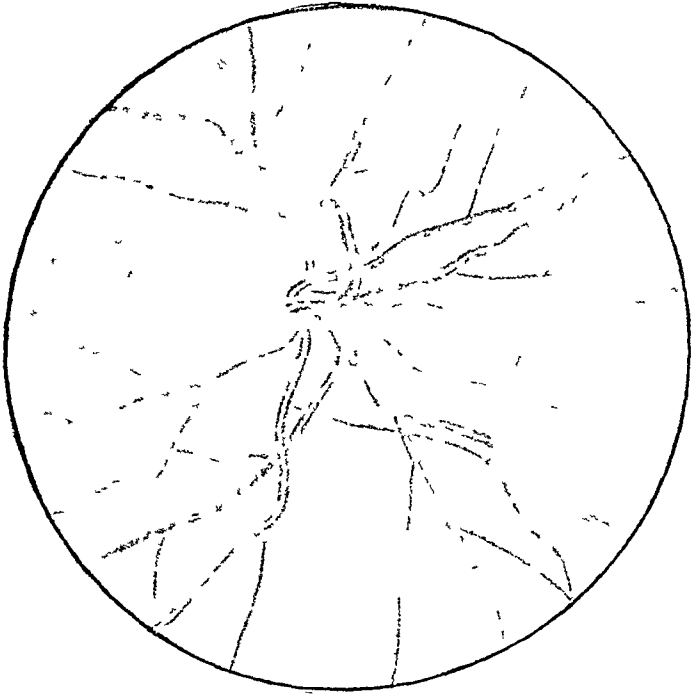


Fig 1 —Fundus in case 1

eyes there was an absolute central scotoma, and the right eye showed metamorphopsia. Both disks were round, the distribution of the vessels was inverse, and at the nasal side of the disk there was a cleancut, yellowish region, $2\frac{1}{2}$ p d wide, where there had evidently been absorption of pigment epithelium. In the macula of the right eye, there was a small Fuchs spot. In the left eye, a some-

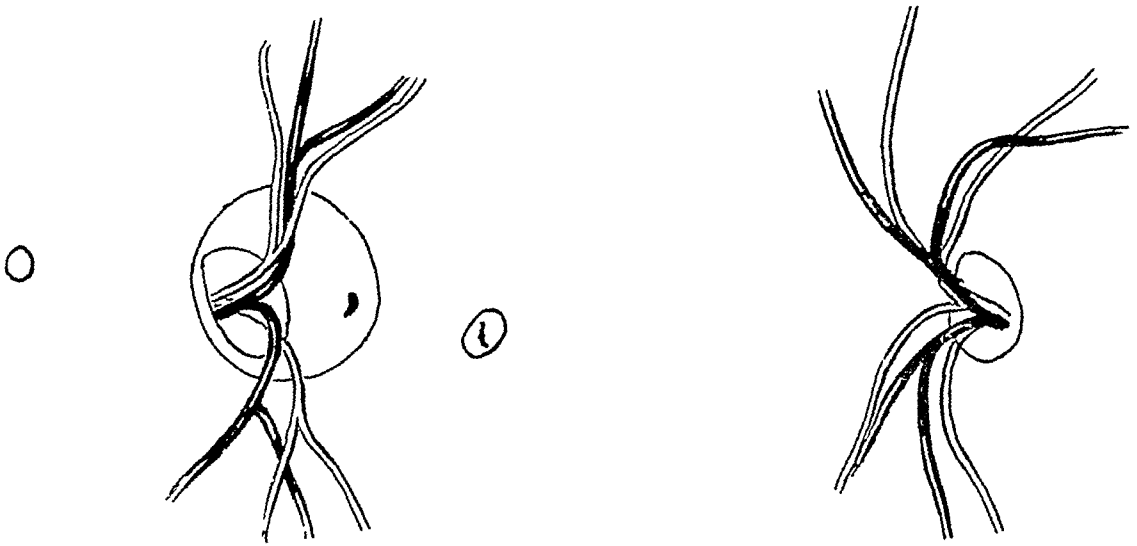


Fig 2—Right eye —8.00 D sph —1.00 D cyl, axis 15, left eye —2.50 D sph —2.00 D cyl, axis 15

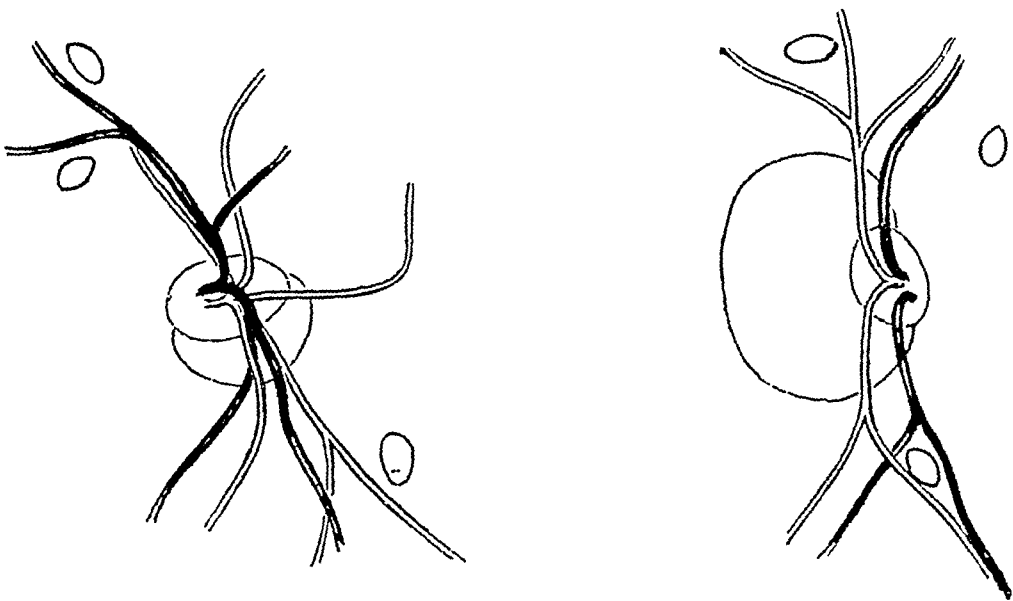


Fig 3—Right eye —2.25 D sph —1.00 D cyl, axis 180, left eye —3.00 D sph —2.50 D cyl, axis 10

what larger, white, cleancut spot was visible in the macula, possibly an old Fuchs spot. An incipient cataract made retinoscopic examination impossible (fig 4).

CASE 5—A middle-aged woman had a correction of —7.00 D for each eye, giving vision of 6/18. Each eye had a slightly vertical oval disk, with an inverse arrangement of the vessels, the disk was surrounded by a clear zone resembling circumpapillary atrophy on the temporal side, where it was rather

narrow On the nasal side, the zone measured $1\frac{1}{2}$ p d Figure 5 *A* shows the left eye One can see a considerable conus of supertraction and a blur of the temporal margin of the disk, as a result of which the atrophic zone appears wider than it really is In the nasal part of the atrophic zone a small retinal artery originates, which, although it does not show a hook or bow at its source, most likely springs from the choroid Nasally the fundus in both eyes was albinotic, strikingly resembling the fundus in a myopic eye and showing in the left eye an atrophic posterior vortex vein In the left eye, 3 p d nasally and below the disk the fundus was very bright, temporally the fundus was reddish brown Retinoscopic examination of the left eye showed a refraction of -4.50 D sph -5.50 D cyl, axis 162 Twenty degrees nasally from the disk the refraction was the same The fovea seemed to be located closer to the temporal margin of the disk than normally The blindspot revealed an enlargement in the right eye in all directions The blindspot of the left eye extended from 9 to 21 degrees (fig 5 *B*) Whereas in all cases previously mentioned an atrophic zone was found chiefly on the nasal side, in the last case a very pronounced circumpapillary zone of

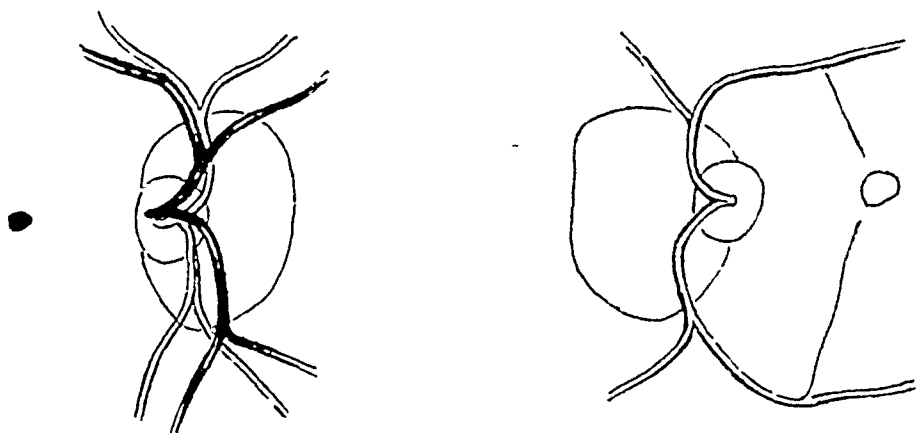


Fig 4—Right eye -4.00 D sph -1.00 D cyl, axis 180, left eye -4.00 D sph

atrophy was present in both eyes, which was greatly extended toward the nasal side An area on the nasal side was distinctly albinotic in type Retinoscopic examination in the horizontal meridian revealed the same refraction nasal to the disk and at the posterior pole, but, as the fundus was especially light nasally and below, one could have been confronted with a high myopia It seems that in this instance the blindspot extended quite a bit closer to the fixation point than normally

CASE 6—A middle-aged woman had 5/5 vision in the right eye with -0.50 D cyl, axis 100 She had an inverse type of arrangement of the vessels, a round disk and a small nasal conus Vision of the left eye was 5/12 with a correction of -5.00 D sph -1.50 D cyl, axis 140 The vessels showed an inverse arrangement, and the disk was vertically oval, looked somewhat smaller than normal and was decidedly dark red It was surrounded by an atrophic zone, rather narrow on the temporal side but nasally over 1 p d in width (fig 6)

CASE 7—A middle-aged woman had a myopia of -5 D in each eye and there was a large nasal atrophic zone, which in the right eye broadened somewhat on top and in the left eye spread out nasally and horizontally In the right eye a cilio-retinal vessel originated at the temporal margin of the disk and extended toward

the macula, while at the lower margin of the disk in the left eye a small, hook-shaped vessel, similar to a cilioretinal vessel, could be seen running downward. Pigmentation was the same on the two sides. The distribution of the vessels was inverse (fig 7).

CASE 8—A man aged 54 had scars on both corneas, which made retinoscopic examination impossible. He had 5/18 vision in the right eye with a -10.00 D lens.

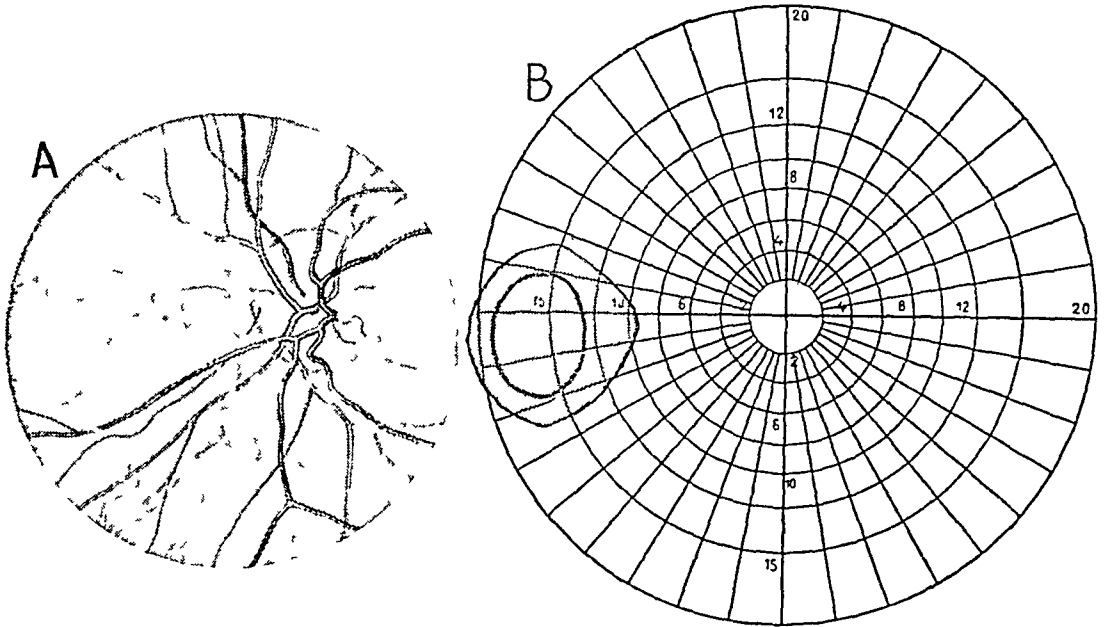


Fig 5—A, fundus of the left eye, B, field of the left eye, with enlargement of the blindspot.

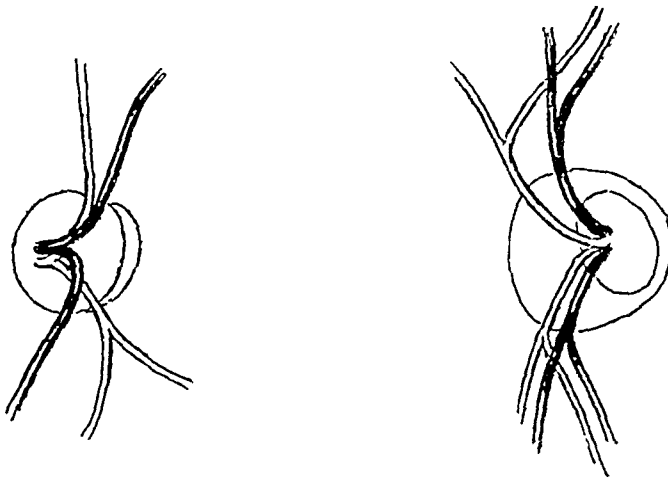


Fig 6—Right eye -0.50 D cyl, axis 100, left eye -5.00 D sph $\subset -1.50$ D cyl, axis 140.

and nasal to the disk there was an atrophic zone 1 p d, wide (fig 8). This eye was extremely divergent. Vision in the left eye was 5/18 with a -7 D lens, and an atrophic zone extended nasally downward from the oblique, oval disk, ending in a pinpoint. The outline of this zone was rather blurred above. The distribution of the vessels was inverse on both sides, and the pigmentation of the fundus was the same throughout.

CASE 9—A man aged 69 had 5/12 vision in the right eye with a -10.00 D $\ominus 1.00$ D cyl, axis 180. There was a normal distribution of the vessels and circumpapillary atrophy, which was more marked on the nasal side than on the temporal. The pigmentation of the fundus was the same in the two eyes. With -1.00 D sph $\ominus 1.50$ D cyl, axis 100, vision in the left eye was 5/6. There was an atrophic zone $1\frac{1}{2}$ p.d. wide at the nasal side. At the upper margin of

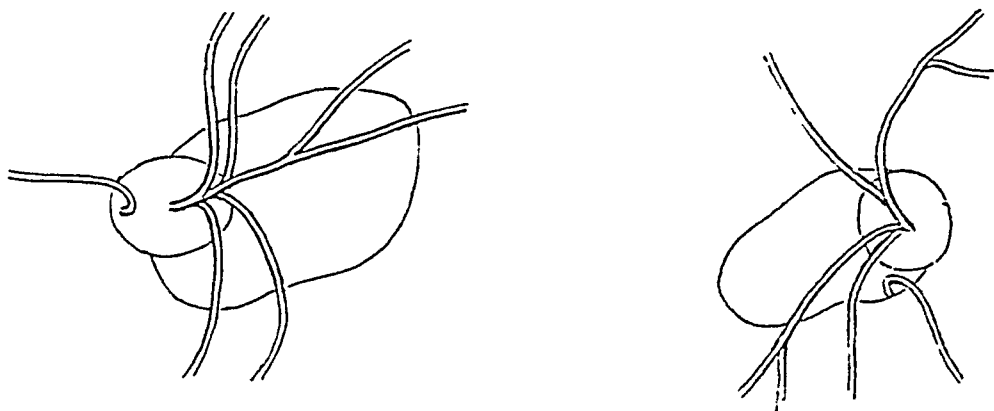


Fig 7—Right eye -5.00 D sph, left eye -5.00 D sph

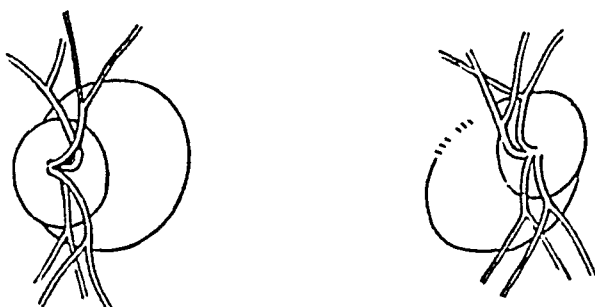


Fig 8—Right eye -10.00 D sph, left eye -7.00 D sph

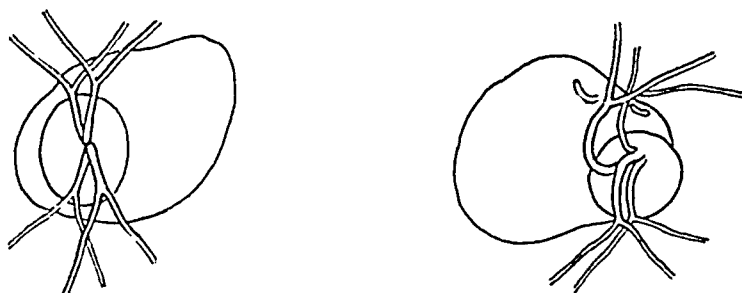


Fig 9—Right eye -10.00 D sph $\ominus 1.00$ D cyl, axis 180, left eye -1.00 D sph $\ominus 1.50$ D cyl, axis 100

this zone heavy choroidal vessels could be seen. The distribution of the retinal vessels was inverse (fig 9). Retinoscopic examination of the left eye gave the following refraction: fovea, -1.00 D sph $\ominus 2.00$ D cyl, axis 100, nasal to the fovea, -3.00 D sph $\ominus 3.00$ D cyl, axis 100, temporal to the fovea, $+0.50$ D sph $\ominus 2.50$ D cyl, axis 115. There existed a slight ectasia of the nasal sclera.

CASE 10—A man aged 31 had $\frac{5}{8}$ vision in the right eye with a correction of -11 D. There was an atrophic zone of the choroid $1\frac{1}{2}$ p d wide on the nasal side. The nasal half of the fundus of each eye was considerably less pigmented than the temporal half. There was an inverse arrangement of vessels in both eyes. Vision in the left eye was $\frac{5}{8}$ with a -10.00 D lens. At the nasal side of the disk there was an atrophic zone $\frac{3}{4}$ p d wide (fig 10). Retinoscopic examination revealed the following refraction: Right eye fovea, -10.00 D, 30 degrees temporally, -6.00 D, 30 degrees nasally, -14.00 D. Left eye fovea, -10.00 D, 30 degrees temporally, -6.00 D, 30 degrees nasally, -15.00 D. There was, therefore, a pronounced ectasia of the nasal scleral region, which was somewhat greater in the eye with the large atrophic zone. The difference in the refraction temporally and nasally was 6 to 8 D, and was consequently considerable.

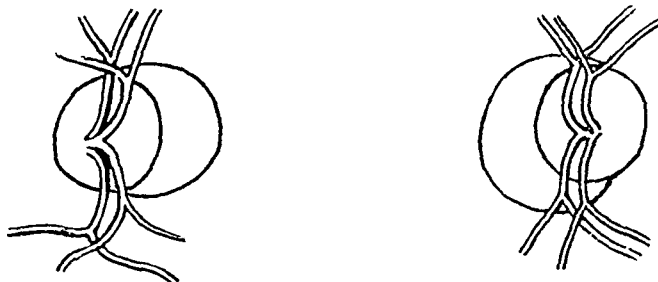


Fig. 10—Right eye -11.00 D sph, left eye -10.00 D sph

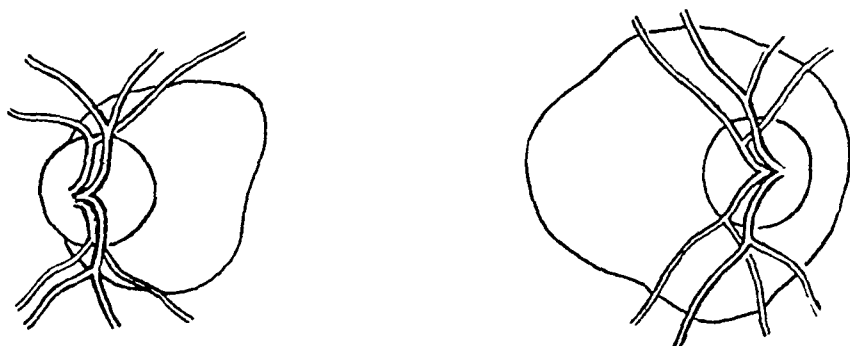


Fig. 11—Right eye -5.00 D, left eye -4.50 D

CASE 11—A man aged 73 had tiny corneal scars on both eyes. Vision in the right eye was $\frac{5}{12}$ with a -5.00 D lens, and nasal to the disk he had an atrophic zone 1 p d in width. In the left eye vision was $\frac{5}{12}$ with a -4.50 D lens (fig 11), and an area of circumpapillary atrophy developed from the nasal atrophic zone, which was $\frac{1}{4}$ p d wide temporally and 2 p d wide nasally. An inverse arrangement of vessels was present in both eyes. The fundus showed only a little difference in the pigmentation between the nasal and the temporal half.

CASE 12—A man aged 42, whose vision was $\frac{5}{5}$ in the right eye with -5.50 D sph $\subset -1.00$ D cyl, axis 50, had a reddish, half-moon-shaped halo nasal to the disk, measuring about 1 p d and bordered by a narrow, whitish band. He had an inverse arrangement of vessels, and the pigmentation of the fundus was the same throughout. In the left eye, vision was $\frac{5}{5}$ with a -5.5 D sph $\subset -1.00$ D cyl, axis 180, and there was the usual temporal conus (fig 12).

CASE 13—A woman aged 30, with a refraction of -10.50 D sph $\subset -1.00$ D cyl, axis 15, in her right eye, had vision of 5/12. There was an atrophic zone, 1 p d wide at the nasal side of the disk, which nearly surrounded the disk. In the left eye, vision was 5/12 with a correction of -9.50 D sph $\subset -1.00$ D cyl, axis 20, and there was a similar atrophic zone, 1 p d wide nasal to the disk, which was wider in the upper than in the lower half. Both eyes had an inverse type of vascular arrangement, and the fundi were albinotic on the nasal side and reddish brown on the temporal side, so that the choroidal vessels were not visible here (fig 13)

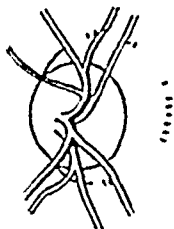


Fig 12—Right eye -5.50 D sph $\subset -1.00$ D cyl, axis 50

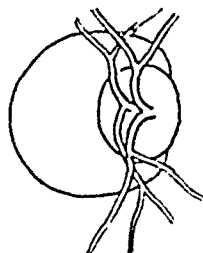
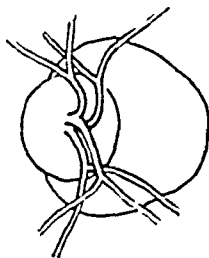


Fig 13—Right eye 0.50 D sph $\subset -1.00$ D cyl, axis 15, left eye -9.50 D sph $\subset -1.00$ D cyl, axis 20

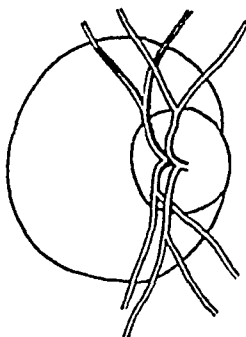


Fig 14—Left eye -11.00 D sph

CASE 14—A woman aged 70 had a mature cataract in the right eye, and in the left eye vision was 5/18 with a correction of -11.00 D. In addition to an incipient cataract and many opacities in the vitreous of the left eye, there was an atrophic zone in the choroid running nasally from the disk, $1\frac{1}{2}$ p d wide, and almost completely surrounding the disk. The vessels were inverse in distribution, and the pigmentation of the fundus was the same throughout (fig 14)

The cases described here are not all that I have seen. They occurred so often that I ceased to make a record of all of them. When I started

to collect data on them in 1926, I made notes of 6 instances of which only two sketches and a colored picture are available. In 1944, I have memoranda on 4 cases (9 to 13). In all these cases I observed an extended light, sharply defined area at the nasal side of the disk, corresponding to what one finds at the temporal side in high myopia. I therefore call this type of change in the fundus "myopia inversa." One is dealing here with a zone in which the pigment epithelium has become atrophic, so that the choroid and sclera shine through with a yellowish or whitish color, and in which the choroid seems to be everywhere atrophic (fig 1). Usually this atrophic zone lies nasal to the disk in a straight line, and only occasionally runs slightly oblique, either nasally and above or nasally and below (figs 7 and 9), but joins the disk on the nasal side. Thus, this zone, with its exact nasal position, is distinguishable from the congenital conus on the nasal side, since the latter rarely lies strictly on the nasal side, but more often is nasal and below. The outline of the nasal zone is usually clear everywhere (fig 12). Only once did it appear intermittently blurred (fig 8). The atrophic zone in myopia inversa generally is considerably larger than one would expect from the amount of refraction. I have never found a small, half-moon-shaped atrophic zone on the nasal side of such a degree as that which one ordinarily sees with myopia of 3 to 4 D, and which is perhaps $\frac{1}{4}$ to $\frac{1}{3}$ p d wide. Often, the nasal zone is rather wide, 1 to 2 p d, and not infrequently the atrophic zone surrounds the disk, analogous to circumpapillary atrophy, as I had an opportunity to observe in 5 cases (figs 2, 5, 6, 9 and 11).

The distribution of the vessels is nearly always inverted. Once (fig 9) I found a normal distribution of vessels in the right eye, which showed circumpapillary atrophy with a marked nasal extension. The myopia of that eye was $-10D$, while examination of the left eye disclosed a myopia of $-1.00D$ $\subset -1.50D$ cyl, axis 100, with a nasal atrophic zone $1\frac{1}{2}$ p d wide and an inverse arrangement of vessels. The circumpapillary zone on the nasal side with a normal distribution of the vessels of the right eye in a case of high myopia leads me to presume that such an instance represents a transition from ordinary myopia to myopia inversa.

Pronounced supertraction of the temporal margin of the disk is not present ordinarily in cases of myopia inversa. In case 5 only was one able to see a certain supertraction of the temporal margin of the disk (fig 5), because this was very hazy and partially covered the vessel funnel. I found pronounced supertraction of the temporal margin in the case shown in figure 15, to which I shall refer later, in this case I found a wide nasal atrophic zone, but no myopia. Also, in a case to be mentioned later one of inferior myopia, the upper margin of the disk was blurred and showed actual supertraction over the disk. Bor-

ders of the nasal zone are generally sharply defined only in one eye (fig 2), the zone appearing reddish and being circled by a white band. In another case (fig 8) part of the zone was not clearly outlined.

The nasal zone is usually homogeneous in color. I once found pigment in this region (fig 2), and at another time choroidal vessels appeared (fig 9), again a vessel originated in the margin of the zone below, which formed a hook and ran down and temporally (fig 7). From its appearance, one can be sure that one is dealing with a condition analogous to a myopic conus and circumpapillary atrophy on the temporal side, and not a congenital anomaly, in these cases in which there is an atrophic zone nasally. Case 2 furnishes convincing proof, in this case a circumpapillary atrophy developed in the patient's thirty-second year from the wide nasal zone which I had previously sketched when he was 14 years old. There was, therefore a progressive change in the fundus.

It is manifest that a genuine nasal conus does not exist in these cases. I have never seen a combination of a typical nasal conus and an atrophic zone. In high myopia there is usually no difference between the temporal myopic conus and an extended temporal or circumpapillary atrophy of the choroid, but there is a great difference between the myopic conus and the nasal conus. A myopic conus develops slowly and becomes wider, usually about the tenth year, while the nasal conus represents a congenital abnormality and usually does not undergo any of the changes similar to those in the inferior conus. The disk was usually vertically oval in cases of myopia inversa (figs 2 and 3) or obliquely oval (case 7), but a white crescent was never visible beside the disk as one finds it sharply defined at the nasal margin. I seldom saw an atrophic zone below like those on the nasal side, which is remarkable since the inferior conus can be found more frequently than the nasal conus. I shall refer to this question later. In the right eye in case 3 the wide conus seen below and inside is a congenital one and can be easily distinguished from the wide atrophic zone on the nasal side.

The fovea appeared to be closer to the disk than it is normally, but examination of the blindspot showed it to be normally distant from the fixation point but a trifle enlarged downward (case 1). As in the case of a real nasal conus, I believe that the fovea is often closer to the margin of the disk than normally. This is generally not true in the case of the nasal atrophic zone. Only in case 5 did the fovea seem to be closer to the temporal margin of the disk, and the enlargement of the blindspot extended from 9 to 21 degrees. The center of the blindspot corresponded, therefore, to the center of its real position.

In 5 cases the pigmentation of the fundus was less pronounced on the nasal than on the temporal side while in the other cases it was the same everywhere. There is, therefore, a pigmentation of the fundus in

these cases similar to that in cases of inferior conus. In case 1 only a minor difference in the pigmentation of the two halves of the fundus existed. In case 5 a considerable difference appeared.

In these cases of myopia inversa the visual acuity varied from 6/6 to 6/60. In a few cases it was better than one usually expects with ordinary myopia of the same degree. In case 10 vision was 5/8, and in case 9 it was 5/12 with a correction of $-10\text{ D sph} \subset -1\text{ D cyl}$, axis 180. The patient was 69 years old, and for a person with myopia of this age such an acuity can be considered very good.

The degree of myopia of the nasal atrophic zone is quite different. What appears conspicuous and important is that the extension of the nasal zone is caused less by the degree of myopia than is the extension of the temporal zone in ordinary myopia. In the latter, one can estimate the approximate amount of myopia from the appearance of the fundus. This cannot be judged, however, from the nasal zone, because with very slight myopia one finds large changes at the disk. In case 4 there was a particularly wide zone with a myopia of 4 D, in case 14, a very large, comprehensive nasal zone with a myopia of 1 D, and in case 3, a zone 2 p d in width with a myopia of $2\frac{1}{2}\text{ D}$. It is interesting to speculate on the width of the atrophic zone in relation to the amount of myopia, which can be done in case 9. In the right eye, a zone of circumpapillary atrophy existed with a myopia of -10 D , which was wider nasally than temporally. The arrangement of the vessels was normal. The left eye showed a wide nasal atrophic zone of $1\frac{1}{2}\text{ p d}$ with inverse type of distribution of the vessels and a myopia of 1 D. One could assume from the width of the atrophic zone that the myopia of the left eye should be at least as high as that of the right eye, and yet it was actually much lower.

One of the clinical characteristics of inverse myopia is an extended atrophic zone at the nasal side of the disk, which has the appearance usual with high myopia. In the course of time this zone may become much larger. Pigment spots and occasional isolated atrophic areas may appear in the fundus. At the same time, the arrangement of the vessels is inverse.

It is strange that this change at the nasal side of the disk associated with myopia has not been described in greater detail. It is not mentioned in the "Kurzes Handbuch der Ophthalmologie". My father mentioned only 1 case which he had observed, and in which there was a nasal half-moon of $2\frac{1}{2}\text{ p d}$ ⁶. He expressed the belief that if the disk had been surrounded and accompanied with atrophic spots it would have corresponded to the ophthalmoscopic picture of the fundus in a case of ordinary high myopia. I cannot say whether these atrophic zones develop as an ordinary circumpapillary atrophy in cases of high myopia,

⁶ Fuchs, E. Arch f Ophth 93:381, 1917

in which a temporal conus first becomes larger and wider and finally encloses the disk, but it is very probable. In case 2, however, in which the patient was observed when he was 14 years old, a very large area of atrophy lay at the nasal side of the disk. In cases of high myopia at this age, such zones can hardly be so well developed. It is remarkable that a difference in refraction exists in the various parts of the fundus, which may very often be found in cases of myopia inversa. In 4 cases (2, 5, 9 and 10) I determined the refraction of the posterior pole of the eye by retinoscopy and that at a distance of 30 degrees nasally therefrom. The refraction in the right eye in case 2, in which a wide and nasal circumpapillary atrophy existed, was 7 D greater nasally than in the posterior pole of the eye. The left eye had also a myopia of approximately 8 D higher on the nasal side, but had no nasal zone, although an inverse arrangement of vessels was present. There is here a peculiar contradiction. The amounts of refraction of the various parts of the fundus are practically the same, whereas the picture of the fundus and the appearance of the disk are entirely different. The right eye had become much more myopic from the fourteenth to the thirty-second year in the case of this patient. The refraction increased from -3.50 to -8.00 D, while the slight myopia of the left eye remained practically unchanged. Therefore, a progressive myopia existed in the right eye, while the myopia in the left eye remained stationary. One could assume that a certain congenital myopia existed in both eyes, together with differences in refraction in the fundus and an inverse type of vessel arrangement, and that the circumpapillary atrophy of the right eye was attributable to the progressive myopia.

In case 9, the difference in refraction between the temporal and the nasal side was $4\frac{1}{2}$ D. In case 10, the difference between the temporal and the nasal side was 8 D in the right eye and 9 D in the left eye, and the difference between the fovea and the nasal side was 4 D in the right eye and 5 D in the left eye. One can see from these findings that there exists an ectasia of the nasal part of the sclera, where the macular regions sometime participate. At other times, the nasal side shows no higher refraction than the temporal parts of the fundus. One might believe that the atrophic zone on the nasal side was caused by this ectasia, but this does not always seem to be the case, for in another instance the refraction at the posterior pole and that of the nasal part of the fundus were equal. In this case, a narrower zone of circumpapillary atrophy existed than in the former case, and the nasal ectasia was not so extensive. The nasal bulge in the sclera does not seem to be the only cause of the atrophic zone on the nasal side of the disk. This is supported by the fact that considerable differences of refraction existed in those eyes in which no conus of the disk was revealed. Rubert⁷ described

7 Rubert Ztschr f Augenh 20 512, 1916

2 such cases in which the disk was normal, except for an irregular type of vessel arrangement, and in which the refraction was considerably higher below than above. In 1 case, refraction showed slight hyperopia, while below the myopia increased to -8.00 D. In the other eye, a slight myopia was found above, while below there was a pronounced myopia. Such cases have rarely been observed, although they probably occur more frequently than one might suppose.

The following case⁸ falls under the head of myopia inversa. A woman aged 32 had had poor vision from childhood and at 14 years of age wore her first pair of glasses, which were only slightly increased later. Her parents and grandparents had not been myopic. The disk and the distribution of the vessels were normal in both eyes. The fundus was reddish brown, but nasally it suddenly became conspicuously tessellated, most likely due to a small amount of pigment in the pigment epithelium. Vision in the right eye was $\frac{5}{8}$ with a -11.00 D lens, in the left eye it was $\frac{5}{8}$ with a -6.00 D lens. The cornea of the right eye had a refractive power of 60.5 D, and that of the left eye, 62 D in the horizontal meridian. In the right eye, retinoscopic examination disclosed a refraction of -11.00 D $\subset -1.50$ D cyl, axis 25, and in adduction of 30 degrees, a refraction of -14.00 D $\subset 0.75$ D cyl, axis 25. In the left eye, retinoscopic examination disclosed refraction of -6.50 D $\subset -1.00$ D cyl, axis 180 at the posterior pole, and in adduction of 30 degrees, a refraction of -9.00 D $\subset 0.50$ D cyl, axis 180. It is apparent that in this case there was a special, congenital myopia, which increased negligibly, which was common but in which the nasal part of the sclera showed a remarkable bulge. There existed neither any abnormality of the disk nor any myopic stretching of the choroid. In myopia inversa, the size of the nasal zone is also remarkable. Why is it so large, even with minor degrees of myopia? The nasal ectasia may cause a special pull of the choroid, because here, between the nasal part of the ora serrata and the disk, there is a much shorter section of the choroid, and so the lamina vitrea and pigment epithelium are subject to more pull than in ordinary myopia, in which the pulling is effective on the temporal side and thus the entire posterior portion of the eyeball is included. As previously stated, in 1 case (case 9) I found no particular bulge on the nasal side on retinoscopic examination, therefore, there must be another important reason for the special pulling on the nasal side. Probably in cases of myopia inversa the optic nerve passes through the sclera in a reverse direction, for there always exists an inverse type of arrangement of the vessels in these cases. Perhaps this exposes the nasal half of the disk more to the pulling.

I must mention a case here (Negrusch) in which the clinical picture approximated that of myopia inversa, only, the myopia was lacking. This

⁸ Fuchs,² p. 169

would contradict the view that a slight extension of the axis with a reversed direction of entrance of the optic nerve has any connection with the origin of the nasal zone. A woman aged 67 had vision of 5/8 with -1.50 D cyl axis 150 in the right eye and of 5/8 with -0.50 D \subset -1.75 D cyl, axis 140 in the left eye. She had marked supertraction of the temporal margin of the disk in both eyes and a very wide and high atrophic zone at the nasal side of the disk in the left eye. The arrangement of the vessels was inverse in both eyes. The pigmentation was the same everywhere, and the fovea was normally distant from the margin of the disk (fig 15). Because of an external disease of the eye, retinoscopic examination could not be performed. The eye presented a perfect picture of myopia inversa, perhaps there was a moderate lengthening of the axis, but this was compensated for by an especially flat lens or by a moderate curvature of the cornea.

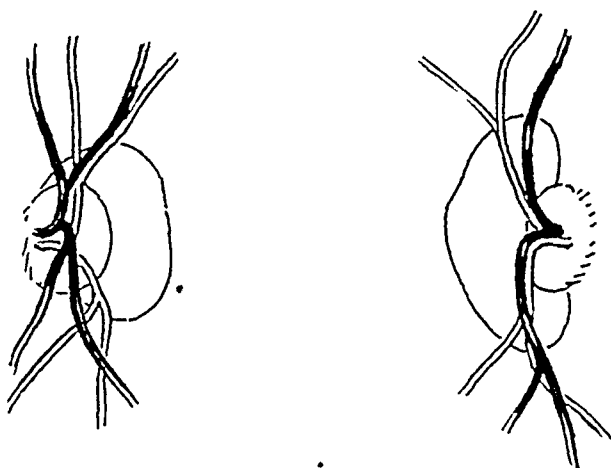


Fig 15—Right eye -1.50 D cyl, axis 150, left eye -0.50 D sph \subset -1.75 D cyl, axis 140

In this connection, I wish to draw attention to these cases in which a similar atrophic zone can be found beneath the disk with myopia. They seem to be rare, and I have a record of only 2.

CASE 1—A man aged 39 had a small, typical inferior conus in his right eye, while in his left eye he had a wide, half-moon-shaped atrophic zone, $1\frac{1}{2}$ p d in width downward and a myopia of 4 D.⁸

CASE 2—A woman aged 56 consulted me because of diplopia. Examination revealed an incipient cataract in each eye, which had produced a monocular diplopia. The right eye had vision of 5/12 with a -4.50 D lens and an inverse arrangement of the vessels, the disk was slightly oblique and oval, and there was a wide atrophic zone of the choroid with a small pigment spot downward, measuring about $1\frac{1}{2}$ p d in width (fig 16). In the left eye vision was 5/12 with a -4.50 D lens, but here the distribution of the vessels was normal. Below the disk, a half-moon-shaped atrophic choroidal zone, $\frac{3}{4}$ p d in width, could be seen with

a longitudinal pigment spot at its margin. In both eyes, the margin of the disk which lay opposite the atrophic zone was blurred and looked like an area of supertraction. There was no difference in the pigmentation of the various parts of the fundus. Retinoscopic examination was impossible because of irregularities of the lens.

It seems to me that this feature, which I might call myopia inferior, is rarer than myopia inversa—a fact which is astonishing, since the real, congenital, inferior conus is so much more frequent than the real, congenital, nasal conus. It would seem that these atrophic zones found at unusual places do not originate from a congenital conus, neither are they the offspring of a genuine conus, nor do they have any connection whatever with them, but they are due to a pull, and this pulling seems to be more frequent nasally than below.

As to the histology of the nasal conus, I found two publications in which, unfortunately, no ophthalmoscopic examination had been done. One record is my father's,⁹ and the other is Salzmann's.⁹ The findings



Fig 16—Right eye —4.50 D, left eye —4.50 D

are very different. In the case of Salzmann the ophthalmoscopic picture showed a temporal conus, in which the optic nerve entered obliquely into the retina. The nasal margin of the porus opticus formed a wide angle, while there was a marked supertraction at the temporal margin, where the lamina vitrea and the limiting tissue far overreached the walls of the porus opticus. In the picture one has the impression that the optic nerve in the porus opticus makes a sort of bend, in which the nerve fiber bundles approach nasally and turn just in front of the lamina toward the nasal side, just behind the cribriform plate. Histologic examination by my father revealed no enlargement of the porus opticus on the nasal side, but showed a conical narrowing. The retina was somewhat drawn over the porus opticus toward the nasal side, the lamina vitrea stopping at the limiting tissue and the ganglion cell layer and the nuclear layer being drawn over the nerve tissue of the disk. At the nasal side, the glass membrane began at the scleral opening, but

⁹ Salzmann, M. Arch. f. Ophth. 143:568, 1941

the pigment epithelium and the external layers of the retina were missing for quite a distance. Thus, one has two different kinds of nasal conus, as well as two similar forms of temporal conus: first, the broadening of the porus opticus where the broadened wall of the canal can be viewed from the front as a white half moon and, second, an atrophy of the pigment epithelium, by reason of which the choroid can be seen as a lighter, rather yellowish half-moon. The latter can also be seen in cases of senile conus at the temporal side. I have seen both forms in the inferior conus.

Salzmann expressed the belief that the nasal conus often is narrow and its outlines are blurred because the nerve fiber layer which passes the nasal margin of the optic foramen is considerably thicker on the nasal side than on the temporal side. The nasal conus is often very narrow and blurred, possibly because the broadening of the porus opticus is only slight. This is not true in cases with an atrophic zone of pigment epithelium, as the illustrations show. In these cases the borders are very sharp. I am not sure whether the nerve fiber layer in a nasal conus is really thicker at the nasal than at the temporal side. This cannot be deduced from figure 6 of Salzmann's article. Perhaps here is a condition similar to that in an inferior conus, in which the retina is thicker at the upper margin of the disk than at the lower.² It has been assumed that the inferior conus has a relation to torsion of the eye, specifically, to the entrance of the optic nerve. It is certain that in an inferior conus the lower half of the disk discloses early pathologic changes in certain diseases just as pronouncedly as the temporal half does in a normally formed disk. I have found this in cases of glaucoma and of atrophy of the optic nerve. In the early stages of glaucoma with an inferior conus, the first depression of the cupping is discovered below, and not temporally.¹⁰ If, in the case of disseminated sclerosis, pallor of the disk sets in and an inferior conus is present, one finds the pallor not in the temporal half, as is usually the case, but below. It seems that in an inferior conus the nerve fiber layer is thicker at the upper margin of the disk than below, for I have seen a Weiss-Otto reflex above and not nasally, where it is usually found.¹¹ This reflex is explained by the thick nerve fiber layer, which produces a prominence at the margin of the disk, and one has to assume that if this reflex is found to be displaced the thickest part of the nerve fiber layer corresponds to it.

It would be advisable to study the distribution of the nerve fiber layer bundles in a nasal conus in the red-free light in order to get a proper idea regarding their distribution and course.

¹⁰ Fuchs,² illus 9, pl 2

¹¹ Fuchs,² illus 1, pl 5

A myopia inversa, with the extended atrophic zone at the nasal side and the inverse type of vessel arrangement, leads one to assume that the distribution of the nerve fiber bundles is different and their course more twisted than is normally the case. The extended nasal atrophic zone in myopia inversa seems therefore to correspond with the observation of my father, namely, that there is a simple atrophy of the pigment epithelium. With regard to the histology of myopia inferior, I have found a record of this rare occurrence by Salzmann. He described the case of a myopia with an inferior conus and an atypical staphyloma in the same direction.¹²

¹² Salzmann, M. Arch f Ophth 54 337, 1902. The original text was not available to me.

A NEGLECTED CAUSE OF SECONDARY GLAUCOMA IN EYES IN WHICH THE LENS IS ABSENT OR SUBLUXATED

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GLAUCOMA developing in an aphakic eye, either spontaneously or following discission of a membrane may be due to one of many factors. Among those most frequently mentioned are delayed reformation of the anterior chamber, prolapse of the iris, incarceration of the lens capsule or iris in the wound, adhesion of hyaloid membrane to the wound and anterior synechia of an iris pillar, each resulting ultimately in extensive peripheral anterior synechias. Increased formation of aqueous from irritation of the ciliary body, such as that resulting from traction during the needling operation, has been postulated. Retained lens cortex or vitreous in the anterior chamber may mechanically block the angle and cause hypertension. The glaucoma may sometimes be secondary to iritis or uveitis.

When the lens is subluxated, it may press the iris forward on one side, so as to block the angle here. When the lens is completely dislocated posteriorly, the glaucoma which sometimes occurs has been considered to be due in some cases to increased formation of aqueous from a ciliary body mechanically irritated by the free-floating lens.

All ophthalmologists are familiar with the fact that when the lens is in situ occlusion of the pupil, with or without iris bombe, often causes secondary glaucoma. It is common experience that this form of secondary glaucoma can be relieved if communication is reestablished between the chambers by transfixion of the iris or by iridectomy, unless the condition has persisted so long that the angle is permanently closed. It is perhaps not so generally recognized that a similar cause for glaucoma can exist in eyes in which the lens is absent or dislocated. It is the purpose of this communication to discuss this type of secondary glaucoma and to present illustrative cases from the literature and from our own experience. Four types can be observed. Though all four types are very similar, the mechanism of the block is slightly different in each, and they can be more easily considered separately.

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1 Aphakic eyes, with or without iridectomy, in which the pupil is blocked by a membrane partly or wholly inflammatory

2 Aphakic eyes, nearly always without iridectomy, in which the pupil is blocked by a herniation of vitreous through it, usually after discission of secondary cataract

3 Eyes in which after intracapsular extraction of the lens the pupil is blocked by adhesion of the iris to the intact hyaloid membrane

4 Eyes with partial or complete subluxation of the lens backward, in which the pupil is blocked by a herniation of vitreous through it

TYPES OF SECONDARY GLAUCOMA ASSOCIATED WITH ABSENCE OR SUBLUXATION OF THE LENS

TYPE 1—*Aphakic eyes, with or without iridectomy, in which the pupil is blocked by a membrane partly or wholly inflammatory*

The first to recognize this type of glaucoma was Bowman,¹ in 1865. He stated

But probably the iris will be found to be more or less bulged forward, showing accumulation of fluid behind it in a space not communicating through the pupil with the anterior chamber. Often this bulging is partial or unequal, occasionally the pupillary margin is thrown aslant by it. It is certain that a puncture of the bulging iris with a broad needle, opening a communication with the anterior chamber, usually suffices to relieve the heightened tension, and to cause a subsidence of the rising inflammation.

Since the original description by Bowman, cases of this type have been occasionally reported in which the glaucoma has been overcome by means of needling,² by transfixion of the iris³ or by iridectomy.⁴

Cases 1, 2 and 3, described in detail in the appended case reports, illustrate type 1, block of the pupil by a membrane.

In case 1 a linear extraction had been done. The pupil was relatively large, since both an iridectomy above and an iridotomy below had been done. There

1 Bowman, W. On Extraction of Cataract by a Traction-Instrument with Iridectomy, with Remarks on Capsular Obstructions and Their Treatment, *Ophth Hosp Rep*, London **4** 332, 1863-1865.

2 (a) Smith, P. On the Pathology and Treatment of Glaucoma, London, J & A Churchill, 1891. (b) Chance, B. Glaucoma After the Extraction of Cataract, *Ophthalmology* **6** 565, 1909-1910.

3 Fuchs, E. Ueber Transfixion der Iris, *Ber u d Versamml d ophth Gesellsch* **25** 179, 1896. Lowenstein, A. Lanzentransfixion, *Ztschr f Augenh* **67** 68, 1929.

4 (a) Rumszewicz, K. Zur Casuistik des Glaucoms nach Staar-Operationen, *Klin Monatsbl f Augenh* **34** 191, 1896. (b) Weeks, J. E. Glaucoma After Cataract Extraction, *Tr Am Acad Ophth* **28** 162, 1923. (c) Piekarska-Miaczynska, M. Ueber das Verhalten des intraokularen Druckes an staroperierten Augen, *Klin oczna* **13** 283, 1934. (d) Rislev, S. D. Glaucoma in an Aphakial Eye Three Years After Extraction, *Am J Ophth* **16** 328, 1899. (e) Smith^{2a}.

was a very thin inflammatory membrane in the pupil. The anterior chamber became steadily shallower as the tension rose, but it was a uniform shallowing and did not at all suggest iris bombe. Under treatment with 2 per cent pilocarpine nitrate and 1 per cent epinephrine hydrochloride, the tension increased from 36 to 48 mm, but this was immediately and permanently relieved, and the anterior chamber deepened, with a simple incision of the membrane.

In case 2 the lens substance had been absorbed after needling in early childhood. The pupil was 3 to 4 mm in size. During the course of active iridocyclitis the anterior chamber became extremely shallow without iris bombe, and tension, which had previously been normal, rose rapidly to 45 mm. The pupil was filled with a membrane. After dissection of the pupillary membrane, the anterior chamber became deep and tension normal. Three months later the anterior chamber again became quite shallow, and this time typical iris bombe was noted. The pupil was again completely occluded by a membrane, and tension was 40 mm. An iridotomy and division of the membrane were done with a knife needle. The next day the anterior chamber was deep and tension normal. When the patient was last seen, twelve months later, there was an adequate pupillary opening, and tension was normal.

A third instance of pupillary block by a membrane is seen in the right eye in case 14. The patient had a mature cataract in the right eye, and acute glaucoma developed, evidently secondary to swelling of the lens. The tension dropped to normal with the use of strong miotics, and eight days after his admission, when the eye was almost quiet, an uneventful intracapsular cataract extraction with iridectomy was done. A violent fibrinous iritis developed within a few days after the operation, it gradually quieted down, leaving a dense inflammatory membrane completely filling the pupil. The pupil became somewhat drawn up. Two months after operation there was no active iritis, although the eye was still slightly congested. The anterior chamber was shallow, and tension, which had previously been rather low, was 34 mm. A double transfixion⁵ of the iris was done near the periphery below. The anterior chamber deepened at once and remained deep, and tension has been normal to date without medication. A needling of the membrane will have to be carried out later.

In the first 2 cases needling of the membrane proved completely effective. Such a procedure is not entirely without risk, however, for if normal vitreous lies just behind the membrane it may press forward through the opening and recreate a pupillary block. In cases 1 and 2 there had been long-standing iritis or uveitis, and quite possibly fluid vitreous. In the third case it was considered wiser to reestablish communication between the chambers by means of transfixion of the iris.

5 Transfixion is done with a broad cataract knife as near the periphery of the iris as possible. The knife is passed through the cornea, and the tip is engaged in the iris and passed through it, keeping the point parallel with the posterior surface of the iris. It can then be pushed back through the iris into the anterior chamber, thus making a second hole in the iris. One should exercise great care to avoid plunging the point of the knife backward into the vitreous, for if this is done the purpose of the operation might be defeated by the openings in the iris becoming blocked by vitreous. Should this occur, a small peripheral iridectomy could be done in another place. Of course, if the iris is in bombé form, the transfixion is easily done, without danger of injuring the vitreous.

before needling the pupillary membrane, in the hope of preventing pupillary block with vitreous when discission is done

TYPE 2—*Aphakic eyes, nearly always without iridectomy, in which the pupil is blocked by a herniation of vitreous through it, usually after discission of secondary cataract*

In most of the cases of this type the glaucoma has followed needling of a membrane after simple extraction, but a few cases have been reported in which a combined extraction had been done.⁶ There is often typical iris bombé. Bowman¹ recommended transfixion of the iris for this type. Von Graefe⁷ was evidently well aware of the danger of this type of secondary glaucoma after needling, for he stated, "One should never do a discission in the presence of a small pupil." Hudson⁸ in 1910, in a brilliant paper, was the first to suggest that the cause of the glaucoma of this type is a blocking of the pupil with vitreous. He made his deductions entirely from examination of enucleated eyes. He found in all cases of this type, in which the eyes were enucleated for intractable glaucoma after needling, that the iris was in bombé form and that the pupil was completely filled with vitreous, which herniated into the anterior chamber. He noted many adhesions between the iris and the vitreous. He recommended transfixion of the iris, as first advocated by Bowman,¹ as the treatment of choice in the early stages and iridectomy, as first advocated by H. Knapp,⁹ in the later stages. In other reports on this type of glaucoma, transfixion of the iris¹⁰ and iridectomy¹¹ have proved equally successful. Doubtless because cases of the type under discussion have been overlooked by us, we are able to present only 3 examples from our own experience. These cases, and 3 important cases from the literature, are given in detail in the appended case reports.

CASE 3 (Urbanek¹²)—After a wide discission of a secondary cataract which developed after linear extraction, the tension of the eye became elevated and the

6 Aschew, H. Die Transfixion der Iris, Arch f Augenh **37** 117, 1898.
Dalén, A. Ueber Glaukom nach Starextraktion, Mitt a d Augenklin d Carolin. med-chir Inst zu Stockholm, 1901, no 3, p 75.

7 von Graefe, A. Beitrage zur Pathologie und Therapie des Glaucoms, Arch f Ophth **15** (pt 3) 224, 1869.

8 Hudson, A. C. Injury to the Vitreous Body as a Factor in the Production of Secondary Glaucoma, Roy London Ophth Hosp Rep **18** 203, 1911.

9 Knapp, H. Ueber Glaucom nach Discission des Nachstaars und seine Heilung, Arch f Augenh **30** 1, 1895.

10 Teale, T. P. Puncture of the Cornea for the Relief of Tension, Brit M. J **1** 404, 1864. Lichtenburg, J. S. Glaucoma Following Cataract Operation, J Missouri M. A **19** 345, 1922. Footnote 6.

11 Mitchell, S. Two Cases of Glaucoma Following Cataract Extraction, Ophth Rec **6** 507, 1897. von Hippel, A. Ueber die dauernden Erfolge der Myopieoperation, Arch f Ophth **49** 387, 1900. Rumszewicz^{4a} Knapp⁹.

12 Urbanek, J. Vorfall des Glaskorpers in die vordere Kammer als Ursache intraocularer Drucksteigerung, Ztschr f Augenh **54** 164, 1925.

iris bulged forward in typical bombe form. Urbanek observed with the slit lamp that vitreous completely filled the pupil and herniated forward so as almost to reach the cornea. After transfixion, the iris rapidly resumed its normal position, tension became normal and remained so during a two year period of observation. Shortly after transfixion of the iris, the vitreous was noted to withdraw somewhat from the anterior chamber, and when the patient was examined two years later vitreous filled only a part of the pupil and projected very little into the anterior chamber. The hole in the iris was still patent. It was Urbanek's opinion that the constant motion of the pupil in expansion and contraction, as well as its undulating motion, had allowed a slight seepage of aqueous, which accounted for the relatively slow development of the glaucoma and the fact that the tension never reached a very high level. He expressed the belief that normal vitreous, at least in certain circumstances, was relatively impermeable to aqueous and could therefore act as a mechanical plug to the pupil, as in the case reported. The large herniation of vitreous into the anterior chamber he believed was explained as follows. The greater pressure in the posterior chamber forced more vitreous into the anterior chamber each time a rhythmic, slight dilatation of the pupil took place, and the herniation of vitreous was gripped and held there by the following pupillary contraction. Thus, more and more vitreous tended to enter the anterior chamber. He noted no vitreous near the angle of the anterior chamber at any time in the case reported.

CASES 4 and 5 (Pereira¹³)—These cases present especially interesting features. In case 4 glaucoma followed discission and presented the same features as those in Urbanek's case. Pereira also observed with the slit lamp that the relatively small pupil was completely filled with vitreous and that vitreous herniated to a considerable extent into the anterior chamber. The iris bulged forward. Cyclodialysis was completely ineffective. Under treatment with atropine the tension gradually fell to normal, but when atropine was withdrawn the iris again bulged forward and the glaucoma returned. The hypertension was permanently relieved by transfixion of the iris. He, like Urbanek, stated the opinion that normal vitreous is relatively impermeable to aqueous.

Case 5 was somewhat different. The patient had had an intracapsular extraction with peripheral iridectomy, but the pupil became drawn up, "presumably from vitreous being caught in the wound." Five weeks after operation the eye became red and the vision blurred. The anterior chamber was very shallow and the tension elevated. Examination with the slit lamp revealed vitreous bulging through the pupil almost to the cornea. With instillation of atropine, the tension became lower, and the vitreous largely withdrew from the anterior chamber. Two months later, after strenuous bodily exertion, the original condition recurred. Pereira assumed that during the strenuous bodily exertion a dilatation of the pupil occurred, which allowed vitreous again to come forward into the anterior chamber, and that this herniation completely filled the pupil when it again contracted. On this occasion atropine failed to relieve the condition, and two posterior sclerotomies likewise failed. Finally, an iridectomy was done, after which the anterior chamber again became deep, and tension was permanently controlled, although there still remained some vitreous herniating into the anterior chamber.

13 Pereira, R. F. Hipertension ocular por prolapso del cuerpo vitreo en la camara anterior despues de la discision de la catarata secundaria, Arch de oftal de Buenos Aires 9 115, 1934, Prolapso del vitreo en la camara anterior y glaucoma despues de la extraccion intracapsular de la catarata, *ibid* 11 409, 1936.

CASE 6—The patient had had an uneventful intracapsular extraction with iridectomy. Convalescence was apparently uneventful except for mild postoperative iritis. Five months after operation the eye still showed a mild iritis, with the pupil occluded by an inflammatory membrane. Five months later tension was 24 mm, and there was a suggestion of forward bulging of the iris below. A wide discission was done. The following day tension was 56 mm and there was iris bombé. The iris was transfixed, and a small subconjunctival incision in the sclera was made. There was considerable hemorrhage into the anterior chamber, which in a few days necessitated paracentesis and irrigation of the anterior chamber on account of increased tension. Thereafter the tension remained normal and the iris resumed its normal contour. Five days after the paracentesis it was noted that vitreous was bulging through the pupil, filling the upper half of the anterior chamber. The eye gradually quieted down and had vision of 20/40 with correction. The patient has been followed for five years and has had no further trouble, the tension always remaining normal. There is no further note in the record relative to the presence or absence of vitreous in the anterior chamber.

CASE 7¹⁴—The patient had had severe uveitis and had many posterior synechias. There was an immature cataract. Tension began to rise, and an intracapsular extraction with broad basal iridectomy was done. After several months the tension became elevated and was controlled for some time with miotics, but eventually a cyclodialysis had to be done. Shortly after operation it was noted that an inflammatory membrane completely filled the pupil and the coloboma except for a space about 2 mm in diameter at the lower border of the pupil. Vitreous began to herniate through this small opening, and eight days after operation vitreous was in contact with the cornea. Tension remained 13 to 16 mm. Three months later it was noted that vitreous filled about three fourths of the anterior chamber and had caused corneal edema in two places. Tension was 26 mm. A single puncture was made in the iris with a cataract knife near the limbus at 2 o'clock. The anterior chamber deepened immediately. It had never been very shallow, but not as deep as in the usual aphakic eye. On the patient's discharge, on the day following the iris puncture, the anterior chamber was deep and vitreous was nowhere in contact with the cornea. The patient has been followed for two months. Tension has remained normal and the anterior chamber deep, and vitreous has withdrawn considerably from the anterior chamber.

CASE 8—In this case an extracapsular cataract extraction with iridectomy had been done. Convalescence had been uneventful except that there was a pupillary membrane, partly capsular, partly inflammatory. Two months after cataract extraction a discission was done and a good opening secured, with resulting vision of 20/25 with glass. Three years later the patient returned to the clinic with a history of severe ocular pain and inflammation, of six days' duration. The eye was severely injected, and the cornea was steamy. The anterior chamber was somewhat shallow, particularly on the sides, and was deeper below. The pupil was slightly drawn up, and the coloboma was rather narrow. Some of the capsule was present in the upper part of the coloboma, but there was a good opening in the lower part of the pupil, through which vitreous was herniating forward, so as to reach almost to the cornea. Tension was 52 mm. A single puncture was made in the iris with a cataract knife near the periphery at the 4 o'clock position. The anterior chamber deepened at once. A single dressing was applied and the patient allowed to return home. Two days later the eye was almost white and quiet, the vitreous had retracted to the level of the

14 This case is reported through the courtesy of Dr Mahlon Easton

iris, and tension was 20 mm. The patient has been followed for two months. Tension has ranged from 23 to 15 mm. The eye has remained quiet, and the vitreous has stayed on the plane of the iris. This case is somewhat unusual in that the block of the pupil with vitreous did not occur until three years after the dissection, and without any obvious cause.

TYPE 3—Eyes in which after intracapsular lens extraction the pupil is blocked by adhesion of the iris to the intact hyaloid membrane

We have been unable to find any cases of this type reported in the literature. Cases, 9, 10, 11 and 12 are reported in detail in the appended case reports. Unfortunately, some of the pertinent details are lacking in the records, but the general pictures are fairly complete.

CASE 9—In this case, one month after an uneventful intracapsular extraction through the round pupil with a small peripheral iridotomy, it was noted that the anterior chamber was quite shallow, but tension was normal. The eye remained somewhat congested. Two weeks later the anterior chamber was still very shallow, and tension was 48 mm. Four per cent pilocarpine nitrate, given every two hours, failed to reduce the tension. The hyaloid membrane bulged slightly through the pupil but was intact. It was noted that the small iridotomy opening seemed to be closed by a membrane. A cyclodialysis failed to relieve the condition. Three weeks later a trephine was done, and the record states that "a small iridotomy was done, and there was some loss of vitreous." Though there is no note in the record to that effect, it is possible that this iridotomy opening was plugged with vitreous. At any rate, the anterior chamber remained shallow, and three days after the trephine operation the tension was 36 mm. During the next two weeks the tension remained elevated. Then cyclodiathermy of the lower half of the globe and posterior sclerotomy in the lower outer quadrant were done. For three weeks, with massage and therapy with miotic drugs, the tension remained normal as determined by palpation and then rose to 36 mm. The anterior chamber remained very shallow. The pupil was 2 to 3 mm in diameter and did not react to light. At this time it occurred to one of us for the first time that the glaucoma might be due to a block between the posterior and the anterior chamber. A small, single puncture in the iris was made. Two days later it was noted that the anterior chamber was definitely deeper and the tension was normal to palpation, but there was an anterior synechia at the site of the puncture, and the hole in the iris seemed to be blocked with blood and exudate. One week after the iris puncture the anterior chamber was again very shallow and the tension was 45 mm. At this time the true nature of the situation was finally recognized. Since the anterior chamber had been shallow for so long, cyclodialysis with basal iridectomy was done. There was no loss of vitreous at operation. On the day following operation the anterior chamber was deep and tension normal. The patient has been under observation for three and a half months since the last operation. The tension has ranged from "mushy soft" to 14 mm, as recorded at the last examination. Doubtless the cyclodiathermy, as well as the cyclodialysis done at the time of the iridectomy, contributed to the relative hypotony, but it is clear from the prompt and permanent deepening of the anterior chamber after the iridectomy that the decisive factor in the final relief of the glaucoma was the reestablishment of free communication between the posterior and the anterior chamber, since cyclodiathermy combined with posterior sclerotomy, and cyclodialysis had previously failed to deepen the anterior chamber or to control the tension. At the last examination it was noted that there was complete posterior

synechia between the iris and the hyaloid membrane, except in the iridectomy coloboma. This adhesion had evidently completely sealed off the posterior from the anterior chamber. In retrospect, it is probable that if at the first sign of glaucoma an adequate transfixion of the iris had been done the condition might have been relieved at the outset and the patient spared a series of fruitless operations.

CASE 10—This case presents somewhat different features. Here, there were a widely dilated, fixed pupil from trauma and an iridectomy upward. In spite of gross loss of vitreous at the time of extraction of the lens, there was never any free vitreous in the anterior chamber after operation. What appeared to be a smooth, intact hyaloid membrane stretched across the pupil and was everywhere in contact with the pupillary margin as far up into the coloboma as could be seen. Fine posterior synechias were present. The anterior chamber was always shallow after extraction of the lens and gradually became more so, until five weeks after operation it was almost flat. The tension steadily rose under treatment with miotics and epinephrine. When iridectomy was done, no vitreous was lost, yet the anterior chamber became generally deep and has remained so, except that the small segment of iris remaining between 1 and 3 o'clock was apparently firmly adherent to the back of the cornea. After iridectomy the hyaloid membrane pulled away somewhat from the iris, and it could be seen that the synechia had been complete. The anterior chamber had remained shallow so long that the angle is doubtless permanently closed in part, and further surgical intervention may be necessary to control the glaucoma. However, the marked reduction in tension and the deepening of the anterior chamber after iridectomy indicate that here, also, there existed a block between the anterior and the posterior chamber.

CASE 11—In this case, after an uneventful intracapsular cataract extraction with iridectomy, the patient was discharged from the hospital with a normal anterior chamber and with normal tension. When he was next seen, about six weeks later, the eye was considerably injected and the anterior chamber was deep. Three days later the anterior chamber was shallow and the tension 35 mm. A 2 per cent solution of pilocarpine nitrate was given, but three days afterward the anterior chamber was extremely shallow and the tension 48 mm. In an attempt to do a paracentesis, very little aqueous escaped, but the iris prolapsed through the paracentesis opening. When an attempt was made to reposit it, a small hole was made in the iris. At this point there was escape of more fluid, and the anterior chamber deepened at once. Thereafter the anterior chamber remained deep, tension was normal, and the eye gradually quieted down. The hole inadvertently made in the iris evidently drained the posterior chamber and reestablished communication between the anterior and the posterior chamber. There is no note in the record of the relation of the pupil to the hyaloid membrane at the time of operation, but subsequently a thin inflammatory membrane in the pupil and posterior synechias were noted. It is probable that the inflammation of the iris had sealed the iris to the hyaloid membrane so as completely to block the pupil.

In the last 3 cases discussed, the true nature of the situation was sooner or later recognized and proper measures were taken, albeit in case 11 accidentally. In case 12, however, the true nature of the process was never recognized.

CASE 12—In the beginning, the situation in case 12 was exactly the same as that in case 9. Intracapsular extraction had been done, with a small peripheral iridotomy. Gradual shallowing of the anterior chamber and onset of glaucoma

followed, the eye remaining always irritable. Many times it was noted that the pupil was still small and did not react to light. Then followed a long series of operations. A subconjunctival keratome incision into the anterior chamber, done twice, posterior sclerotomy, cyclodialysis, trephination, paracentesis, and cyclodiatomy, done twice. When the patient was last seen, the tension was 42 mm, and vision equaled 3/200.

In the beginning of the glaucoma in this case it was noted that the pupil was small and immobile. In the light of the other cases reported, it is probable that the pupil was blocked by adhesions between the iris and the hyaloid membrane. It should be noted that in none of these 4 cases did the iris take on the typical bombe form. There was a general uniform shallowing of the anterior chamber. In none was there a herniation of vitreous through the pupil. At most there was a slight forward bulge of the intact hyaloid membrane into the pupil. It is probable that there must be considerable postoperative inflammation in these cases to seal the iris to the hyaloid membrane and that this could be avoided if the pupil were kept dilated. All these eyes were noted to be irritable for some time after operation. The small peripheral iridotomy openings in cases 9 and 12 were evidently blocked by inflammatory membrane or by vitreous.

TYPE 4—*Eyes with partial or complete subluxation of the lens backward, in which the pupil is blocked by a herniation of vitreous through it*

A great many reports of glaucoma due to a dislocated lens are to be found in the literature, but the role of the vitreous acting as a block of the pupil in these cases has apparently not hitherto been clinically recognized, though Hudson,⁸ reporting on the pathologic examination of enucleated eyes, correctly deduced the mechanism of the glaucoma. He examined 2 eyes that had been enucleated for glaucoma and noted in each a subluxation of the lens with herniation of the vitreous through the pupil. The iris was everywhere pushed forward so as to block the angle, but the block of the angle was most complete on the side of backward subluxation of the lens. The clinical details of these cases were not available, but he concluded that the glaucoma must have been caused by the pupil being blocked by vitreous, this resulting ultimately in a flat anterior chamber and complete block of the angle.

Another of Hudson's cases was that of a woman aged 43 who had a severe contusion of one eye. On examination nine days later, the pupil was dilated, the lens was completely dislocated into the posterior chamber, the iris was in bombe form and the tension was elevated. Two paracenteses and a cyclodialysis failing to relieve the tension, the eye was enucleated. Pathologic examination showed iris bombe, with the angle completely closed. Vitreous completely filled the pupil and herniated forward into the anterior chamber. The vitreous was everywhere in close contact with the pupillary margin and showed numerous adhe-

sions here Hudson stated the belief that in this, as in his other, cases the glaucoma had been due to the pupil being blocked by vitreous. Cases 13 and 14, reported in detail in the appended case reports, illustrate this type.

CASE 13—In this case, the upper nasal border of a hypermature cataract was subluxated backward, and vitreous was presenting in the pupil between the iris and the lens. There was prominent exfoliation of the lens capsule. On the patient's first admission, the anterior chamber was observed to be deep except in the lower outer quadrant, where it was shallow peripherally, evidently from a forward tilting of the lens here. Tension was 42 mm. Presumably, the increased tension was due to a partial closure of the angle in the lower outer quadrant and to the capsular exfoliation, since it quickly responded to treatment with 4 per cent pilocarpine nitrate and 0.5 per cent physostigmine salicylate. On his second admission, twelve days later, the anterior chamber was almost flat, but the shallowing was uniform, there was no sign of iris bombe. The lens was seen to be well back of the plane of the iris. Tension was 48 mm, and the eye was extremely injected and painful. Owing to the edematous cornea and the extreme shallowness of the anterior chamber, it was not possible to identify vitreous in the pupil, but it was assumed that vitreous must be present and acting as a plug. When transfixion of the iris was done, aqueous gushed out along the knife blade even before it was withdrawn from the eye, the anterior chamber at once became deep and has remained so. The eye rapidly whitened, and tension remained normal without treatment until three weeks later, when it was found to be 30 mm. The holes in the iris made by the transfixion were patent, the anterior chamber was everywhere deep except, as before, in the periphery of the lower outer quadrant. Some vitreous was still present in the pupil. Pilocarpine was prescribed, and since that time tension has been under 30 mm when the patient has used the miotic faithfully.

CASE 14—In this case the lens was completely dislocated backward, and the cause of the glaucoma was less clear. The anterior chamber was slightly shallow, about the same as in the other eye, in which the lens was in situ. It was somewhat shallower than in the usual aphakic eye. With the slit lamp it could be seen that vitreous was in the pupil and that it practically filled the anterior chamber. It was thought at first that the cause of the glaucoma was probably a mechanical block of the angle by vitreous. The tension, however, had risen from 25 to 57 mm in two weeks under miotic therapy. It seemed possible, therefore, that a block of the pupil by vitreous might be a factor in the glaucoma, especially since the anterior chamber was not as deep as one would expect in such an eye. A relative increase in pressure in the posterior chamber from a blocked pupil would also explain the large amount of vitreous in the anterior chamber. It was decided, therefore, to do a transfixion of the iris, at least, as a preliminary measure. When this was done, the anterior chamber deepened at once. When air was introduced into the anterior chamber and later allowed to escape, the vitreous following was found to be of normal consistency. Postoperatively atropine was given, but this dilated the pupil only to a diameter of 5 mm. The anterior chamber remained deep and the tension normal until two weeks after the operation, when a tension of 30 mm was found. A miotic was prescribed, which has controlled the tension to date. Two weeks after the transfixion of the iris it was noted that there was no vitreous in the anterior chamber, except one strand, 2 to 3 mm in diameter, extending through the pupil and up to the corneal wound. One week later only a very narrow strand, not more than 1 mm

in diameter, remained. It would seem, therefore, that the mechanism of the glaucoma in this case, as in case 13, was a block of the pupil by vitreous. The block probably developed more gradually than in case 13 and never became complete. Such an assumption would explain the more gradual onset of the glaucoma, the large amount of vitreous in the anterior chamber, and the fact that the anterior chamber never became extremely shallow.

COMMENT

In all four types of cases the shallowing of the anterior chamber may ultimately result in mechanical closure of the angle. Hence it is important that the proper treatment be instituted early, before permanent adhesions are formed. If one excepts cases of shallow or flat anterior chamber, due to leakage at the wound, there seems to be no cause for progressive shallowing of the anterior chamber in an aphakic eye, or one in which the lens is partially or completely dislocated backward, other than lack of free communication between the posterior and the anterior chamber. Typical iris bombé, when present, at once suggests a blocked pupil. However, in cases in which there is no such condition, but only a general, or uneven, shallowing of the anterior chamber, as in several cases already discussed, the true situation is not so obvious.

Furthermore, a dense pupillary membrane may have such firm adherence to the iris peripheral to the pupillary border as to prevent a general shallowing of the anterior chamber. In such doubtful cases a transfixion of the iris can be carried out as a diagnostic procedure. Case 6 illustrates the hazard of a wide dissection in the presence of a completely blocked pupil and increased tension in causing a marked herniation of vitreous into the anterior chamber and a block of the pupil by vitreous. A preliminary transfixion of the iris in this case, such as was done in the right eye in case 14, would have equalized the pressures in the posterior and anterior chambers and would in all probability have prevented the marked herniation of vitreous into the anterior chamber following the dissection, with its unfortunate consequences. If a pupil is completely blocked with a membrane partly or wholly inflammatory, it would seem wise always to precede the dissection by a peripheral transfixion of the iris.

In cases of subluxation of the lens, the glaucoma may often be due to a tilting forward of one side of the lens, pressing the iris forward here and blocking the angle, since peripheral anterior synechias thus formed in one place may spread around the periphery until enough of the angle is closed to cause glaucoma. Smith^{2a} and Lawford,¹⁵ among others, have made pathologic reports on such eyes. Except for the pathologic observations of Hudson,⁸ already referred to, the possibility of a block of

¹⁵ Lawford, J. B. Cases of Dislocation of Crystalline Lens, *Ophth. Hosp. Rep.*, London **11** 327, 1886-1887.

the pupil by vitreous in some of these cases has apparently never previously been considered. In most of the reports the presence or absence of vitreous in the pupil is not recorded, and often the depth of the anterior chamber is not noted. Hegner,¹⁶ however, without recognizing the importance of his observations, noted in several of his cases a generally shallow or flat anterior chamber, and in some he observed vitreous occupying the space between the lens and the edge of the pupil. The observations in his cases 8, 9 and 12 bear a striking resemblance to those in our case 13. In his cases 8 and 9 the eye was enucleated, and in case 12 vision was reduced to light perception from glaucoma. It is probable that in these cases, as in many others reported in the literature, a block of the pupil by vitreous was the essential factor in producing the glaucoma.

In cases of complete luxation of the lens backward, shallowing of the anterior chamber on one side when the lens lies against the ciliary body and iris may possibly be a factor in the glaucoma, as in case 1 reported by Lawford.¹⁵ In most other cases reported, however, it has been assumed that the cause of the glaucoma was increased secretion from the ciliary body, due to irritation by the lens, hence, lens extraction has been almost universally employed in treatment. Evidence is lacking, however, that such hypersecretion actually takes place. In the majority of cases of posterior luxation the lens is well tolerated in the vitreous chamber, and no glaucoma occurs. Indeed, Suker¹⁷ reported a case of posterior luxation of the lens of thirty years' duration, with normal tension and preservation of 20/40 vision.

In Lawford's¹⁵ case 3 the patient had had no trouble with the eye for twelve years after the lens became dislocated, then intractable glaucoma developed and the eye had to be enucleated. Pathologic examination showed a deep anterior chamber and an open angle. The anterior chamber was filled with a "soft semi-transparent effusion." The lens lay on the retina posterior to the ora serrata. There was an aggregation of cells in the meshes of the pectinate ligament and about Schlemm's canal, which the author thought might retard the outflow of aqueous. One wonders whether the "coagulated, soft semi-transparent effusion" in the anterior chamber, which microscopically consisted of a "very fine fibre-network with some faintly granular material," was not vitreous, and whether its presence in the anterior chamber was not the cause of the glaucoma. In Hegner's¹⁶ case 11, of posterior dislocation, there were at first a flat anterior chamber and a tension of 70 mm.

16 Hegner, C. A. Klinische Untersuchungen über die Prognose der intra-bulbaren Linsluxationen, Beitr. z. Augenh. 9 707, 1914-1915

17 Suker, G. F. A Dislocated Lens in the Vitreous of Thirty Years Standing in One Eye, Ophth. Rec., 1902, p. 462

Examination some time later revealed that the anterior chamber was deep and that vitreous was herniating through the pupil into the anterior chamber. Tension was 43 mm. It may be that in our case 14 a shallow anterior chamber had preceded the marked herniation of vitreous into the chamber. Possibly, in the later stages the important factor in the glaucoma is mechanical block of the angle by vitreous, which has been forced into the anterior chamber by increased pressure in the posterior chamber as a consequence of pupillary block by vitreous.

After intracapsular extraction one frequently observes some herniation of vitreous through the pupil, evidently due to lack of support by a weak hyaloid membrane. Such prolapse of the vitreous usually does not completely fill the pupil and shows little tendency to continue to advance into the chamber. If, however, the pupil is completely blocked by vitreous and there is no free communication between the chambers, such as is afforded by a patent peripheral iridectomy opening, one may observe a progressive accumulation of vitreous in the anterior chamber to the point of almost completely filling it, with resulting glaucoma.

When free communication is reestablished between the chambers as a result of transfixion of the iris or iridectomy, there is apparently a strong tendency for the vitreous to withdraw from the anterior chamber, as illustrated in cases 3, 4, 5, 7, 8 and 14. Therefore, transfixion of the iris or iridectomy would seem to be indicated, even if the anterior chamber is deep, if it is filled with vitreous. In fact, the withdrawal of vitreous from the anterior chamber as a result of transfixion of the iris or iridectomy may explain the relief of glaucoma in cases in which obstruction to the outflow of aqueous has been due to vitreous in the angle rather than to closure of the angle by forward displacement of the iris. That vitreous filling the pupil offers sufficient obstruction to the flow of aqueous to cause glaucoma is proved, in our opinion, by the dramatic fall in tension which follows transfixion of the iris or iridectomy.

Whatever other causes for glaucoma may operate in cases of backward dislocation of the lens, it seems certain, in the light of Hudson's pathologic report and our clinical observations, that a block of the pupil by vitreous must often be a factor. The presence or absence of vitreous in the pupil or in the anterior chamber can easily be verified by examination with the slit lamp. If vitreous is seen to be herniating through the pupil and the tension is elevated, a transfixion of the iris should be carried out, at least as a preliminary measure. In eyes previously treated by iridectomy and removal of the lens from the vitreous, with relief of the glaucoma, it is possible that the important factor was the iridectomy, which reestablished free communication between the chambers and not the removal of the lens *per se*.

SUMMARY

A form of secondary glaucoma in aphakic eyes and in eyes with dislocated lenses is discussed, in which the causative factor is apparently a block between the anterior and the posterior chamber

This block may be from a membrane partly or wholly inflammatory, from a herniation of vitreous through the pupil acting as a plug or from adhesion of the iris to an intact hyaloid membrane

Treatment should be directed toward reestablishment of communication between the chambers by the use of a mydriatic, by discission of a pupillary membrane, by transfixion of the iris or by iridectomy

It is important that proper treatment be undertaken early, before permanent peripheral anterior synechias are formed

A block of the pupil by vitreous in an aphakic eye, or one with posterior dislocation of the lens, with resultant increased pressure in the posterior chamber, is the probable cause of large accumulations of vitreous in the anterior chamber

In an aphakic eye, or in one with a backward dislocation of the lens, the development of iris bombé, a general or uneven shallowing of the anterior chamber or an increasing accumulation of vitreous in the anterior chamber probably indicates that there is a block between the chambers and that glaucoma is imminent, if it is not already present

In aphakic eyes in which the pupil is completely blocked by a membrane, partly or wholly inflammatory, it is advisable to do a preliminary transfixion of the iris before undertaking a discission of the membrane

In view of our experience in cases 13 and 14, it is probable that the heretofore not clinically recognized block of the pupil by vitreous in eyes with posterior dislocation of the lens is the chief cause of the glaucoma and that in many cases of this type which have been reported in the literature the glaucoma could have been relieved by transfixion of the iris or by iridectomy

REPORT OF CASES

CASE 1—F S, a girl aged 13

May 29, 1939—There was a history of arthritis and of chronic inflammation in both eyes for four years, with gradual loss of vision. Examination revealed low grade uveitis in both eyes, with many posterior synechias and some pupillary membrane, early band keratitis and immature cataract, iris bombé was present in the left eye. Vision was 1/200 in the right eye and 20/100 in the left eye. Tension was 17 mm in the right eye and 30 mm in the left eye

June 28—Iridectomy was done on the left eye

March 22, 1942—The patient was admitted for extraction of the lens of the left eye. Each eye showed moderate band keratitis, a normal anterior chamber, many old posterior synechias, a pupillary membrane and mature cataract. In the left eye there was a coloboma of the iris upward from a previous iridectomy. (Examination with the slit lamp revealed no cells in the aqueous of either eye)

and no precipitates on the back of the cornea) Tension was normal to palpation in both eyes Vision was ability to see shadows, with accurate light projection, in each eye

March 3—A linear cataract extraction with iridectomy upward and inferior iridotomy was performed on the left eye After a moderately stormy convalescence, the eye became quiet, with a clear pupil, and vision with a lens equaled 20/20—This vision has been maintained, and there has been no further trouble with this eye

September 22—Lens extraction with a small iridectomy upward and inferior iridotomy was performed on the right eye There were some postoperative hyphema and moderate inflammation Atropine was used continuously after the operation

October 19—Vision was 20/70 in the right eye with a +10.00 D sphere and a pinhole disk There was a thin pupillary membrane, the anterior chamber was very shallow, and tension was 36 mm Use of atropine was discontinued, and 2 per cent pilocarpine nitrate and 1 per cent epinephrine hydrochloride were prescribed

October 26—Vision was 20/50 + 2 in the right eye with a +10.00 D sphere and a pinhole disk The eye was moderately injected, with slight corneal edema, a very shallow anterior chamber and tension of 45 mm Admission to the hospital was advised

November 2—The patient was admitted to the hospital Tension was 48 mm in the right eye

November 4—With a Ziegler knife, the pupillary membrane was divided with a single vertical incision The next day the anterior chamber was deep and tension was normal Since that time tension has ranged from 10 to 18 mm, without medication

Subsequent Course—The patient was last seen on Jan 14, 1946 Tension was then 18 mm in the right eye, and vision in that eye with glass was 20/20—

CASE 2—O F, a woman aged 23

Jan 10, 1941—There was a history of congenital cataract of both eyes and several needling operations in early childhood The left eye was convergent, the anterior chambers were of normal depth, and the pupils were slightly irregular and 3 to 4 mm in diameter, with good central openings Tension in both eyes was normal to palpation Vision with glass was 20/200 in the right eye and 4/200 in the left eye

April 30, 1943—The right eye was quiet, with many precipitates on the back of the cornea, a thin pupillary membrane and opacities in the vitreous

Feb 18, 1944—The right eye showed many keratic precipitates

October 18—The right eye was considerably injected, the anterior chamber was of normal depth, the pupil was small and nearly filled with inflammatory membrane Tension was normal to palpation

November 21—The patient was admitted to the medical ward with a questionable diagnosis of rheumatic fever While she was in the ward the right eye remained inflamed Treatment consisted of instillations of atropine and application of hot compresses On account of the medical condition, foreign protein and salicylates were not given

December 11—The patient began to suffer acute pain in the right eye Examination showed an extremely shallow anterior chamber Tension was 45 mm A dissection of the pupillary membrane was done and a small opening secured The following day the anterior chamber was normally deep and tension was

normal She was discharged from the hospital on Jan 4, 1945, with the eye still somewhat inflamed but with normal tension

March 20, 1945—The right eye was slightly injected, the anterior chamber was very shallow, the iris was of bombé form, and the pupil was occluded with inflammatory membrane Tension was 36 mm

March 21—With a Ziegler knife, an iridotomy and division of the pupillary membrane were done At the time of discharge, on March 27, the anterior chamber was normal in depth except in the region of a few peripheral anterior synechias Tension was normal

April 10—Tension was 15 mm in each eye

June 8—Tension was normal to palpation

Subsequent Course—The patient was last seen on Jan 18, 1946 Vision with glass was 18/200 in the right eye The pupillary opening was good, the anterior chamber was normal in depth, and there were several peripheral anterior synechias Tension was 18 mm

CASE 3—F M, a youth aged 17 (Urbanek¹²)

Oct 26, 1921—Right Eye The anterior chamber was normal, congenital zonular cataract was present, vision was 6/24

Left Eye The anterior chamber was deeper than that of the right eye The pupil was slightly oval and smaller than the pupil in the right eye A pupillary membrane was present Vision was limited to counting fingers at 1 meter

October 28—Operation was performed on the left eye With two needles, a wide opening was made in the pupillary membrane

October 29—A wide central pupillary opening was present in the left eye

November 1—The patient was discharged from the hospital At the time of discharge the eye was slightly injected, the anterior chamber was fairly deep in the pupillary zone, but in the periphery it was slightly shallower than before operation The pupil was round and slightly more than half dilated, with a wide opening and vitreous bulging through the pupil into the anterior chamber Vision was 6/12 with glass

November 16—The patient returned to the clinic with pronounced ciliary injection of the left eye The cornea was cloudy He had been suffering some pain for several days Tension to palpation was slightly elevated There was iris bombé Examination with the slit lamp showed a large herniation of vitreous into the anterior chamber, reaching almost to the cornea in the central zone The vitreous completely filled the pupil, and the pupillary border of the iris seemed everywhere in close contact with it The angle of the chamber appeared to be free Tension was 35 mm Vision with glass was 6/18

November 18—A transfixion of the iris was done and the anterior chamber deepened at once

November 19—The eye was white and the cornea clear

November 20—The anterior chamber was deep and there was less vitreous in it

November 27—The contour of the iris was flat Vitreous had almost completely withdrawn from the anterior chamber but still filled the pupil Tension was 25 mm in each eye The patient was discharged

Nov 23 1923—The patient was reexamined He had had no further trouble with the eye The pupil was slightly oval horizontally and reacted well in the upper and lower portions There was no adhesion anywhere between the iris and

the vitreous. The hole in the iris at the site of the transfixion was patent. The fundus was normal. Vision with glass was 6/12.

CASE 4—F J, a man aged 25 (Pereira¹)

Aug 10, 1925—The patient had a history of injury to the left eye with a piece of steel while working with a hammer and chisel. The right eye was normal. Examination of the left eye showed ciliary injection. A 3 mm perforating wound of the cornea lay just inside the limbus at 7 o'clock. The anterior chamber was shallow nasally and superiorly. The lens was opaque, with its matter bulging into the anterior chamber from a wound in the capsule. Tension was higher in this eye than in the right eye. Atropine and cold compresses were prescribed.

September 10—Tension was normal. The lens matter was being absorbed.

April 1926—Only a little of the lens capsule remained in the temporal part of the pupil, between 2 and 7 o'clock. The rest of the pupil was black. The fundus was normal. Vision with glass was 6/8.

1931—A thick secondary membrane was observed in the pupil. Vision was limited to counting fingers at 15 meter.

April 1933—Vision was limited to counting fingers at 5 meters.

September 1933—The left eye was divergent. Vision with glass was limited to counting fingers at 6 meters. The fundus was not visible.

Sept 18, 1933—Dissection was done with two needles, resulting in a wide opening in the capsule. A large herniation of the vitreous occurred into the anterior chamber. Atropine was prescribed.

September 22—Vision with glass was 6/8.

September 30—There was acute glaucoma in the left eye, with severe pain. The cornea was steamy, the iris was of bombe form, tension was elevated. A subconjunctival injection of 0.2 cc of epinephrine hydrochloride (1:1,000) was given. Atropine and a 3 per cent cocaine ointment were prescribed, and the patient was placed flat in bed, lying on his back.

October 1—Tension was still elevated. Cyclodialysis was done between the 7 and 12 o'clock position. Use of atropine was continued.

October 5—Tension was high. Instillation of atropine was continued. The tension gradually fell.

December 10—The patient went back to work but returned the same night with acute glaucoma in the left eye and severe pain. The eye was intensely injected, the cornea was steamy, the pupil was small, vitreous was almost in contact with the cornea, and the pupil was filled with vitreous. Iris bombe was present. With use of atropine and a cocaine-epinephrine ointment, tension was quickly reduced.

December 14—Double transfixion of the iris was performed temporally with a Graefe knife. The anterior chamber quickly became deeper, the cornea cleared, and tension fell to normal.

December 20—The patient was discharged. The cornea was clear. An anterior synechia was present at 3 o'clock. The anterior chamber was deep everywhere except at the site of the anterior synechias. The vitreous retracted so that it was less than half the distance from the pupil to the cornea. The iris was on a flat plane. The transfixion holes in the iris were patent.

CASE 5—A M, a man aged 67 (Pereira¹⁸)

June 15, 1931—The patient was admitted to the hospital with a history of failing vision of one year. Examination showed nuclear cataract in each eye.

Vision was limited to counting fingers at 0.75 meter in the right eye and was 6/18 in the left eye

June 16—Intracapsular cataract extraction with peripheral iridectomy was performed on the right eye

June 17—The anterior chamber was flat, the pupil was half dilated

June 20—The anterior chamber was formed

June 29—The patient was discharged from the hospital. There was ciliary injection, the cornea was clear except for folds in Descemet's membrane, the pupil was drawn upward, so that the upper part of the iris disappeared behind the scleral overhang. There was a separation of the choroid nasally. Vision was 6/24 with glass.

July 22—The patient was readmitted to the hospital. Two days before admission he had vomited during the night. The following morning the eye was inflamed and painful and the vision blurred. The right eye showed ciliary injection. There was uveal tissue in the temporal part of the wound. The cornea was clear, the anterior chamber deep and the pupil drawn upward and half dilated. There was a large hernia of vitreous into the anterior chamber, which reached the cornea in the central zone. Tension was +1. Vision with glass was 6/12. The patient was kept in bed, lying on his back, and atropine was prescribed.

July 24—There was slight injection. The vitreous had receded to the plane of the pupil. Tension was normal. Vision with glass was 6/18.

September 26—After twelve days of hard work at cutting wood, the patient had experienced intense pain in the right eye, and it had become inflamed. Examination of the right eye showed ciliary injection and a cloudy cornea. The anterior chamber was very shallow, being absent at the periphery. The iris was congested. The pupil was dilated and drawn upward. The vitreous was herniated through the pupil, was in contact with the cornea in the central zone and reached the angle in some places. Tension was elevated. Vision with glass was limited to counting fingers at 0.5 meter. The patient was put to bed on his back and atropine prescribed.

September 28—The condition was unchanged. Tension was 60 mm.

September 29—A posterior sclerectomy in the inferior temporal quadrant was done, with escape of a moderate amount of fluid vitreous. The eye failed to improve, and another posterior sclerectomy was done in the inferior nasal quadrant. After this the tension fell a little, and finally an iridectomy was done. There was moderate bleeding into the anterior chamber.

October 12—The hyphema was absorbed. There was slight congestion. The cornea was clear except for precipitates on the posterior surface. There were cells in the aqueous. The anterior chamber was deep. Iridodonesis was present. Tension was normal. There was a large coloboma of the iris upward, through which vitreous bulged into the anterior chamber. The disk was pale, with slight excavation. Vision with glass was 6/15.

Pereira expressed the belief that during the strenuous physical exertion the pupil had probably become dilated and vitreous had then come forward into the anterior chamber and was strangulated there on later constriction of the pupil.

CASE 6—S H, a woman aged 67

June 23, 1939—There was immature cataract in both eyes. Vision was limited to counting fingers at 8 feet (240 cm) in the right eye and was 20/70 with glass in the left eye. Tension was normal in both eyes.

September 30—Combined intracapsular cataract extraction was done on the right eye. Convalescence was complicated by mild, but prolonged, iritis with membrane formation. There was no elevation in tension.

December 4—Refraction revealed vision of 20/50 with lens in the right eye and 20/40 with lens in the left eye.

March 22, 1940—Both eyes were white and quiet. Tension was 20 mm in the right eye and 22 mm in the left eye.

July 19—Both eyes were white and quiet. The right eye showed a thin pupillary membrane with complete posterior synechia and suggestive early iris bombe. Tension was 24 mm. Vision with lens was 20/100 in the right eye.

August 10—A wide dissection of the membrane was done on the right eye. The day following operation the tension became elevated to 56 mm and iris bombe was present.

August 11—With a cataract knife, the iris in the right eye was transfixed, and a small subconjunctival scleral incision was made. A large hyphema followed this procedure. Tension remained low for three days.

August 15—Tension was 56 mm in the right eye. Paracentesis was done, and part of the blood was removed. After this the tension fell and remained between 12 and 15 mm until the time of the patient's discharge. The blood was gradually absorbed. It was noted that vitreous was bulging through the pupillary opening, filling the upper half of the chamber.

August 23—The patient was discharged from the hospital.

Subsequent Course—She was seen repeatedly until Dec 14, 1945, and tension was found to vary from 14 to 20 mm. Vision with lens was 20/40. There was slight cupping of the disk.

CASE 7—J A P, a man aged 62

Jan 15, 1941—Vision was 20/50 in the right eye and 20/70 in the left eye. Posterior synechias and immature cataracts were present in both eyes. Tension was 24 mm in the right eye and 45 mm in the left eye. Pilocarpine nitrate, 2 per cent, was prescribed, to be used four times a day in the left eye.

January 27—Tension was 30 mm in the right eye and 40 mm in the left eye. Pilocarpine nitrate, 4 per cent, was instilled once a day in the right eye and five times a day in the left eye.

February 11—Tension was 22 mm in the right eye and 35 mm in the left eye. Physostigmine ointment was added to the medication, to be used each night in the left eye.

March 18—A combined intracapsular cataract extraction was done on the left eye. (Operation was preceded by a course of typhoid vaccine.) Convalescence was uneventful.

September 8—Tension in the right eye had again started to rise. A combined intracapsular cataract extraction was therefore performed on that eye. (Operation was again preceded by a course of typhoid vaccine.) Again, convalescence was satisfactory. Subsequent vision was 20/15 in the right eye and 20/100 in

the left eye The poor vision in the left eye was due to glaucomatous changes Tension in both eyes remained satisfactory until the winter of 1942, when it became slightly elevated in both eyes Miotics controlled the tension for a time

Feb 2, 1943—An acute exacerbation of glaucoma occurred in the right eye The patient was hospitalized and treated with miotics, which reduced the tension satisfactorily

March 2—The patient was discharged, with instructions to use pilocarpine nitrate, 2 per cent, every three hours in the right eye and four times a day in the left eye Since this time vision in the left eye has been between 20/100 and 20/200, with a reduced field of vision The tension has remained satisfactory Vision in the right eye remained 20/20, with a normal field but with borderline tension (20 to 30 mm), until the fall of 1945

Sept 17, 1945—Two days before, the patient had a strenuous day and experienced a spell of blurred vision Tension was 29 mm in the right eye and 22 mm in the left eye Treatment was continued unchanged

November 14—Blurring and halos were experienced in the right eye The cornea was steamy, with a few posterior synechias Tension was 37 mm Furmethide (furfuryl trimethyl ammonium iodide), 1 drop, was instilled in the right eye for four doses at fifteen minute intervals The tension was unchanged The patient was admitted to the hospital and given an intensive course of treatment with miotics, which reduced the tension to 29 mm Gonioscopic examination showed the angle to be free except in the upper nasal quadrant, where anterior synechias could be seen

November 19—Cyclodialysis was performed on the right eye, one third of the angle being opened

November 20—A thin membrane covered the surface of the vitreous, with a very small opening in its inferior aspect, through which vitreous had herniated

November 24—The patient was discharged from the hospital, with instructions to use 2 per cent pilocarpine nitrate three times a day in the right eye

November 27—Vitreous had herniated through the aforementioned opening sufficiently to be in contact with the cornea in one place below the pupillary border Tension was 10 mm in the right eye and 20 mm in the left eye Pilocarpine medication was stopped in the right eye and continued in the left eye

December 4—Examination revealed essentially no change Vision was 20/30—in the right eye

Feb 28, 1946—The vitreous had herniated farther into the anterior chamber of the right eye, so that it filled about three quarters of the anterior chamber and was in contact with the cornea over a considerable area, with two points of corneal edema There was bulging of the iris at the 2 o'clock position Tension was 26 mm in the right eye, and vision was 20/40—Operation was advised but the patient requested postponement

March 14—With the Graefe knife, transfixion of the iris of the right eye was done in the 2 o'clock position Considerable aqueous escaped, more than could have been present in the anterior chamber alone The anterior chamber which had previously been slightly shallower than would be expected in an aphakic eye, deepened in its inferior portion

March 15—The entire anterior chamber was deeper than previously The vitreous was no longer in contact with the cornea The patient was discharged with instructions to use 1 per cent atropine twice a day (Pilocarpine treatment was continued in the left eye)

March 19—There was some injection of the right eye. The vitreous had withdrawn further. Tension was 19 mm in the right eye. The use of atropine was continued.

March 26—The right eye was somewhat irritable, probably from atropine. The eye felt softer, but the tension was not taken because of the irritability. The vitreous was further retracted. Atropine medication was discontinued.

April 2—The right eye was white and quiet. The vitreous was unchanged, it filled about one-half the anterior chamber in the pupillary area and was not in contact with the cornea. Tension was 18 mm in the right eye.

April 16—Tension was 17 mm and vision 20/30 in the right eye.

May 27—Tension was 13 mm in the right eye. There was possibly a little more vitreous in the anterior chamber.

CASE 8—L. S., a woman aged 65

Sept 25, 1912—An immature cataract was present in each eye. Vision was 1/200 in the right eye and 4/200 in the left eye.

November 14—Combined intracapsular cataract extraction was done on the right eye. Convalescence was uneventful. Final vision with glass was 20/20. This vision has been maintained to date.

November 21—Extracapsular cataract extraction with iridectomy was done on the left eye. The convalescence was uneventful except that there was a pupillary membrane, partly capsular and partly inflammatory.

Jan 30, 1943—Dissection was done on the left eye. A good opening was obtained. Subsequent vision with glass was 20/25.

Feb 23, 1946—The patient returned to the clinic with a history of severe pain and inflammation in the left eye, with loss of vision of six days' duration. The left eye was considerably injected, the cornea was steamy. The anterior chamber was somewhat shallow, particularly on the sides. It was deeper below. The pupil was slightly drawn up, and the coloboma of the iris was rather narrow, about 4 mm. Some of the capsule was present in the top of the coloboma and along the nasal border. The pupil was clear in the lower central portion, with vitreous herniating through it so as to reach almost to the cornea. Vision with glass was 15/70. Tension was 52 mm. A single puncture was made with a broad cataract knife in the periphery of the iris at the 4 o'clock position. The anterior chamber deepened immediately. A single dressing was applied, and the patient was allowed to return home.

February 25—The left eye was almost white and quiet. The anterior chamber was deep. The vitreous had withdrawn from the anterior chamber, and its anterior surface was on the plane of the iris. Tension was 20 mm. No local treatment was given.

March 2—The left eye was white and quiet. Tension was 23 mm.

March 11—Tension was 14 mm in the left eye.

March 25—Vision with glass was 20/40—1 in the left eye. Tension was 15 mm. The anterior chamber was slightly shallow temporally. The vitreous was bulging slightly through the nasal third of the pupil.

April 22—Tension was 16 mm in the right eye and 15 mm in the left eye. In the left eye, the vitreous was on the plane of the iris all over the pupil except for a very slight bulge on the nasal side. In several places there seemed to be a space between the iris and the vitreous.

CASE 9—A D, a man aged 68

June 11, 1945—On the patient's admission to the hospital, the right eye was aphakic, with iridectomy upward. The media were clear, and the fundus was normal. Vision with glass was 20/30 in this eye. The anterior chamber of the left eye was normal and the pupil round and active. Vision was 20/200 in this eye.

June 12—Intracapsular cataract extraction, with a small peripheral iridectomy, was done on the left eye. There were no complications.

June 14—The anterior chamber was good. The pupil was round and central. There was moderate redness.

June 19—The patient was discharged. Atropine was prescribed. Vision with a +12.00 D sphere and a pinhole disk was 20/30—

June 25—The left eye was moderately injected. The cornea was clear. Sutures were removed.

July 16—The anterior chamber of the left eye was rather shallow. There was moderate injection.

July 30—The left eye was moderately injected. The anterior chamber was shallow. The pupil measured about 2.5 mm. The hyaloid membrane was on the plane of the iris. Tension was 48 mm. Four per cent pilocarpine nitrate was prescribed.

July 30—Tension was 48 mm in the left eye. Vision with a +12.00 D lens and a pinhole disk was 20/30. Vitreous was bulging somewhat through the pupil, but the hyaloid membrane was intact. The iridectomy opening seemed closed with a membrane. The anterior chamber was very shallow. The patient was admitted to the hospital.

August 3—Cyclodialysis was done on the left eye, between 6 and 9 o'clock.

August 4—Tension was 36 mm in the left eye. A 4 per cent solution of pilocarpine nitrate and physostigmine ointment were prescribed.

August 8—Tension was 36 mm in the left eye.

August 13—The patient was discharged. Tension was 28 mm in the left eye.

August 20—The patient was admitted to the hospital. Vision in the left eye with a +12.00 D lens and a pinhole disk was 20/30— Tension was 48 mm. The anterior chamber was very shallow.

August 25—Trephination was done on the left eye, with a small iridectomy. Vitreous was lost at operation.

August 28—The anterior chamber was rather shallow. Tension was 36 mm. Four per cent pilocarpine nitrate and 1 per cent epinephrine hydrochloride were given, and daily massage of the eye was prescribed.

September 5—Tension was 35 mm in the left eye.

September 11—Tension was 45 mm in the left eye.

September 11—Cyclodiathermy of the lower half of the circumference of the eye and posterior sclerotomy in the lower outer quadrant were performed.

September 12—The anterior chamber had become a little deeper. The eye was soft after massage.

September 19—Tension was 18 mm in the left eye. The anterior chamber was a little deeper than before but was still rather shallow. The pupil was small. The vitreous showed a great deal of opacity. Vision equaled accurate light pro-

jection The patient was discharged from the hospital Four per cent pilocarpine nitrate was prescribed

September 24—The left eye was still rather red The pupil measured 2 mm and was fixed to light The anterior chamber was very shallow There was some blood in the pupil Tension was normal to palpation Atropine was prescribed

October 1—The anterior chamber was very shallow The pupil was small A posterior synechia was present Tension was 36 mm The patient was admitted to the hospital

October 2—A single small puncture was made in the lower outer quadrant of the iris

October 4—Tension was normal to palpation The tiny puncture in the iris seemed to be filled with blood and fibrin, and iris was adherent to the back of the cornea here The anterior chamber was somewhat deeper than before

October 8—Tension was 45 mm in the left eye

October 9—A small cyclodialysis was done in the upper nasal quadrant, and a broad basal iridectomy was done through the cyclodialysis wound No vitreous was lost Moderate bleeding occurred into the anterior chamber

October 10—The anterior chamber was deep

October 17—The anterior chamber was deep Nearly all the blood had gone from the anterior chamber The eye was "soft"

October 22—The eye was "soft" Vitreous was bulging somewhat into the anterior chamber Atropine was prescribed

November 5—The left eye was "soft" Atropine medication was continued

November 10—Tension was 10 mm in the left eye Atropine medication was discontinued The vitreous was clearing

December 3—The left eye was "soft"

December 24—Tension was 18 mm in the left eye, and the eye was still moderately injected

Jan 21, 1916—Examination of the left eye showed a few cells in the aqueous, a little blood around the margin of the coloboma of the iris and many adhesions between the iris and the hyaloid membrane, forming a complete synechia except in the coloboma Many coarse opacities were seen in the vitreous The eye was nearly white and quiet The disk was slightly pale No pathologic cupping was present Tension was 14 mm Vision with glass was 20/50

February 4—Tension was 19 mm in the right eye and 15 mm in the left eye Both eyes were white and quiet There was no pathologic cupping, but the left disk was slightly paler than the right The anterior chambers were deep A few large opacities were present in the vitreous of the left eye Only a little blood clot remained around the border of the coloboma in the left eye

March 4—Tension was 18 mm in the right eye and 14 mm in the left eye In the left eye, the posterior synechia between the iris and the hyaloid membrane was complete everywhere except in the operative coloboma

April 1—Tension was 17 mm in the right eye and 14 mm in the left eye Examination showed no change

CASE 10—L V, a man aged 50

Feb 16, 1945—Three months prior to admission the patient had been struck in the left eye with a blunt piece of metal He was said to have had a severe

intraocular hemorrhage with glaucoma, necessitating irrigation of the anterior chamber to remove the blood

Right Eye Vision was 20/20, and the eye was normal

Left Eye The eye was slightly injected There was a scar about 6 mm long in the cornea near the limbus at 12 o'clock, with iris adherent to it The pupil was slightly drawn up, about 6 mm horizontally and 8 mm vertically It reacted to light The lens was in position above and tilted slightly backward below, with vitreous presenting in the space between the iris and the lens The lens showed considerable opacity The aqueous showed a few cells, and the beam of the slit lamp was slightly visible Tension was normal Vision was 6/200 Atropine was prescribed

During the next few months the eye gradually became quiet and the lens completely opaque

September 7—Operation was performed on the left eye Two corneal sutures were used An upward incision was made with a Graefe knife, and the anterior synechia was cut through in making the section, producing a fairly large coloboma of the iris upward and leaving some iris attached to the cornea Normal vitreous presented immediately, and the lens was delivered in capsule with a wire loop There was considerable loss of vitreous A large bubble of air was put into the anterior chamber The chamber formed the day after operation The patient was discharged on the seventh day after operation, and atropine was prescribed There was considerable postoperative inflammation, and the anterior chamber remained very shallow

October 5—The eye was almost white The anterior chamber was extremely shallow No free vitreous was present in the chamber What appeared to be a hyaloid membrane stretched across the pupil Tension was 25 mm Atropine medication was discontinued

October 15—The anterior chamber was extremely shallow Hyaloid membrane was in contact with the cornea in the upper central zone The pupillary border was everywhere in close contact with the hyaloid membrane, even as far up into the coloboma of the iris as could be seen Many fine synechias were present between the iris and the hyaloid membrane The pupil was in the same state of dilatation as at the first examination and did not react to light Tension was 38 mm Four per cent pilocarpine nitrate was ordered

October 18—Tension was 40 mm The eye was otherwise unchanged The patient was admitted to the hospital for operation A conjunctival incision was made in the lower outer quadrant and a flap dissected up toward the limbus A scratch incision about 6 mm long was made through the sclera parallel to, and about 5 mm back of, the limbus A spatula was introduced and a small cyclo-dialysis opening made Iris forceps were introduced into the anterior chamber, the iris was drawn out through the scleral wound, and a broad iridectomy was done No vitreous was lost Considerable bleeding occurred into the anterior chamber The next day the anterior chamber was deep, as in the usual aphakic eye, and tension was normal Considerable blood was present in the chamber The patient was discharged on the sixth postoperative day At discharge gross blood was gone from the anterior chamber The chamber everywhere was deep except where the strip of iris between the upward coloboma and the recent iridectomy was in contact with the back of the cornea

October 31—Tension was 27 mm The patient was given physostigmine and epinephrine and told to massage the eye

November 9—Tension was 17 mm

November 16—Tension was 19 mm Four per cent pilocarpine nitrate and 1 per cent epinephrine hydrochloride were prescribed

Subsequent Course—The patient was seen at weekly or semiweekly intervals until January 18 At these visits, except for two readings of 30 mm, tension remained 25 mm or less The anterior chamber remained deep, the eye became quiet There was moderate opacity of the vitreous, and no cupping of the disk

It is probable that the angle is sufficiently blocked by anterior synechia from the long-continued extreme shallowness of the chamber so that further operation will ultimately be necessary permanently to control the tension

CASE 11—L C, a man aged 66

March 11, 1945—Immature cataract was present in both eyes Vision was 20/70 in the right eye and 20/50— in the left eye

June 17—An uneventful intracapsular cataract extraction with complete iridectomy upward was performed on the right eye Two corneoscleral sutures were used The anterior chamber formed on the day following operation The patient was discharged on the ninth postoperative day and given atropine.

August 6—The patient did not report back to the clinic until this date At this visit the eye showed considerable injection and slight striate keratitis There was a good anterior chamber There were numerous opacities in the vitreous, so that details of the fundus were not made out Examination with the slit lamp was not carried out The patient complained of some pain in the eye. There was no note of tension

August 9—The patient returned with severe pain in the right eye The anterior chamber was extremely shallow, especially temporally, where the iris seemed to be in contact with the cornea The corner showed epithelial edema Many cells were noted in the aqueous and many opacities in the vitreous Tension was 30 mm Two per cent pilocarpine nitrate was prescribed

August 12—The patient was admitted to the hospital, with marked injection of the right eye, a steamy cornea and an extremely shallow anterior chamber, which seemed to be flat temporally He was suffering from severe pain Tension was 48 mm Paracentesis was done through the cornea in the 10 o'clock position with a Graefe knife When the knife was withdrawn, the iris prolapsed through the wound When an attempt was made to replace it, a hole was inadvertently made in the iris, and a gush of watery fluid escaped through the wound The iris was then easily repositioned The following morning the eye was described as "mushy soft" The anterior chamber was deep Atropine was prescribed and its use continued during the stay in the hospital Intravenous injection of typhoid vaccine was given on two occasions The eye slowly quieted down, and the patient was discharged on the eighteenth postoperative day Tension remained normal and the anterior chamber deep Atropine medication was continued at home

September 13—There was slight ciliary injection The anterior chamber was deep There was a thin pupillary membrane, and numerous cells were noted in the aqueous Atropine medication was continued

October 8—The right eye was practically white and quiet A rare cell was present in the aqueous Use of atropine was discontinued

November 19—The right eye was white and quiet A thin pupillary membrane was present Tension was 20 mm

Feb 18, 1946—Vision with a +10.00 D lens and a pinhole disk was 20/30—1 in the right eye Tension was 19 mm

February 27—Refraction of the right eye was done, and vision with glass was 20/30

CASE 12—P F, a man aged 59

Jan 31, 1944—An immature posterior cortical cataract was present in both eyes Vision was 2/200 in the right eye and 20/40 in the left eye

March 7—Intracapsular cataract extraction with peripheral iridectomy was done on the right eye There was no loss of vitreous or other complication The anterior chamber was formed on the first postoperative day, and convalescence in the hospital was uneventful The patient was discharged on the ninth postoperative day Atropine was prescribed

March 27—The eye was moderately red

April 17—There was a history of pain for five days The right eye was moderately red The pupil measured 3 mm The cornea was edematous The anterior chamber was shallow There were a few cells in the aqueous Tension was 48 mm A Reese incision was made into the anterior chamber

April 20—Tension was 49 mm in the right eye Another Reese incision was made

April 25—Posterior sclerotomy was done in the upper nasal quadrant

April 29—Tension in the right eye was normal to palpation The anterior chamber had become slightly deeper

May 1—Tension was 42 mm in the right eye The eye was considerably injected The pupil measured 3 to 4 mm and was fixed to light The anterior chamber was moderately shallow Vision was 3/200

May 8—The anterior chamber was moderately deep There was no pupillary reaction to light A few cells were present in the anterior chamber "Vitreous was also present" Tension was 36 mm

May 16—Cyclodialysis was done in the lower outer quadrant

May 19—Tension was 65 mm

May 20—A trephine opening was made in the upper inner quadrant, with a small iridotomy There was no loss of vitreous

May 22—Tension was 22 mm

May 24—Tension was 40 mm

May 25—Tension was 36 mm With massage and use of 1 per cent epinephrine hydrochloride, tension gradually fell to normal, and the patient was discharged June 3

June 12—Tension was 36 mm Use of 4 per cent pilocarpine nitrate was continued

June 26—Tension was 30 mm A small infiltrated ulcer was noted in the lower portion of the cornea, with a hypopyon measuring 3 mm The pupil was here described as being drawn somewhat upward and nasally, so as to give the appearance of a complete coloboma The anterior chamber was deep With intravenous injections of typhoid vaccine and local administration of penicillin, the ulcer gradually healed Tension became higher, however, and on June 30 a paracentesis of the anterior chamber was done

July 4—Tension was 40 mm

July 5—Cyclodiathermy was done on the temporal side

July 11—The patient was discharged from the hospital. Tension was normal to palpation. Determinations of tension were made as follows:

Date	Tension, Mm
July 17	17
July 24	22
July 31	22
August 14	"Eye still red"
September 11	15

September 12—Cyclodiathermy was done at the 7 to 10 o'clock position.

September 30—The patient was discharged from the hospital. The right eye was soft to palpation. Determinations of tension were made as follows:

Date	Tension
October 16	Very soft
November 6	Very soft
December 4	Very soft

Jan 8, 1945—Tension was 22 mm in the right eye, and vision with glass was 6/200. During the next several months the right eye remained quiet, and tension was usually 22 mm or less.

December 10—Tension was 42 mm, and vision was 3/200.

CASE 13—J. T. H., a man aged 87.

Dec 21, 1945—The patient was admitted to the hospital with a history of pain and blurred vision in the right eye for forty-eight hours. The right eye was considerably injected, the cornea steamy and the anterior chamber deep, the pupil was about 2 mm and was fixed to light. The iris was tremulous. There was a hypermature cataract, which was subluxated backward and slightly nasally, and vitreous was bulging into the nasal part of the pupil. There was marked exfoliation of the lens capsule. Tension was 42 mm. Vision equaled accurate light projection. The left eye was white and quiet, the anterior chamber was deep, and the pupil was about 2.5 mm and reacted to light. There was an immature cataract. Vision was 20/100. Tension was 16 mm.

During the day of admission the right eye was given intensive treatment with 4 per cent pilocarpine nitrate and 0.5 per cent physostigmine salicylate. At 8:30 p. m. tension in the right eye was 32 mm. While the patient was in the hospital, 4 per cent pilocarpine nitrate and 1 per cent epinephrine hydrochloride were used in the right eye four times a day. Tension remained normal, and he was discharged December 26, with instructions to follow the same treatment.

December 31—Tension was 18 mm.

Jan 5, 1946—Tension was 19 mm.

January 7—The patient was readmitted to the hospital with a history of severe pain in the right eye for eighteen hours. The eye was intensely injected, the cornea was steamy, the anterior chamber was almost flat, and the pupil measured 3 mm and was fixed to light. On account of the steamy cornea, it was difficult to tell whether there was vitreous in the pupil. The lens appeared to be 2 or 3 mm behind the plane of the iris. Tension was 46 mm.

An operation was done, consisting of a double transfixion of the iris in the upper portion with a Graefe knife. There was considerable escape of aqueous, and the eye became soft.

January 8—The anterior chamber was deep and tension was normal. No treatment was given.

January 10—Tension was 17 mm The patient was discharged from the hospital without treatment

January 14—The cornea was clear, the anterior chamber deep and the vitreous bulging through the pupil on the nasal side The lens was tilted backward nasally The two holes in the iris were open, but there was an anterior synechia at the site of the nasal hole

January 28—Tension was 30 mm The right eye was moderately injected The anterior chamber was deep except for an anterior synechia at the site of the nasal one of the two iris punctures Both holes were patent The chamber was also slightly shallow at the periphery inferotemporally The pupil was about 3 mm, vitreous filled the pupil but did not project into the anterior chamber

It was felt at this examination that the slightly increased tension was due to shallowing of the anterior chamber peripherally in the lower temporal quadrant from the backward tilting of the lens, together with the shallowing incident on the formation of the anterior synechia at the site of the temporal puncture and the presence of exfoliation of the lens capsule In view of this, it was felt that the glaucoma should now be favorably influenced by a miotic The patient was given 2 per cent pilocarpine nitrate to use four times a day

February 11—Tension was 26 mm in the right eye and 17 mm in the left eye Examination revealed no change

February 25—Tension was 28 mm in the right eye and 15 mm in the left eye Pilocarpine nitrate, 4 per cent, was given four times a day in the right eye

March 25—Tension was 34 mm in the right eye and 15 mm in the left eye The right eye was essentially unchanged in appearance, vitreous still filled the pupil The anterior chamber was everywhere deep except in the lower outer quadrant The pupil was 3 mm and fixed Exfoliation was marked The patient had neglected to use drops They were again ordered

April 22—Tension was 24 mm in the right eye and 20 mm in the left eye With the slit lamp, a little vitreous was seen protruding slightly into the anterior chamber through the lower half of the pupil Medication with 4 per cent pilocarpine nitrate was continued

CASE 14—J M, a man aged 75

Jan 29, 1945—Right Eye The cornea was clear, the anterior chamber was slightly shallow, the pupil was round and active, an immature cataract was present, with marked exfoliation of the lens capsule, and tension was normal to palpation Vision was 11/200

Left Eye The eye was slightly convergent, the anterior chamber was deep, the lens was completely dislocated posteriorly and lying down behind the iris below, the fundus was normal Tension was normal to palpation Vision with a cataract glass was 20/30 Glasses were prescribed

December 31—The patient complained of blurred vision in the left eye The disk was slightly pale, but no pathologic cupping was noted Vision was 20/70 with glass Tension was 25 mm Two per cent pilocarpine nitrate was prescribed

Jan 7, 1946—Vitreous was noted in the anterior chamber Tension was 46 mm Admission to the hospital was advised

January 14—The patient was admitted to the hospital The right eye was unchanged, tension was 17 mm

Left Eye The anterior chamber was almost normal, possibly slightly shallow, and of about the same depth as that of the right eye Examination with the slit lamp showed vitreous in the pupil and nearly filling the anterior chamber

It was thought to be normal, since it was tremulous. Tension was 57 mm. Vision with glass was 20/200.

January 15—Operation was performed on the left eye. A double transfixion of the iris was done in the upper portion with a Graefe knife, and the eye immediately became soft. A large bubble of air was introduced into the anterior chamber, since this made the eye hard, it was evacuated. When the air was evacuated, it was followed by a bead of vitreous, which was pulled out and excised. Atropine was prescribed.

January 16—The anterior chamber of the left eye was rather deep, tension was normal.

January 17—Tension was 18 mm. in each eye.

January 18—Tension was 17 mm. in each eye.

January 19—The patient was discharged. The anterior chamber in the left eye was rather deep and was nearly filled with vitreous. The pupil was about 3.5 mm. Tension was 14 mm.

January 22—Tension was 16 mm. in the right eye. The left eye still showed moderate injection. The pupil was 3 to 4 mm. Tension was 23 mm. Atropine medication was continued.

January 28—Tension was 19 mm. in the right eye and 30 mm. in the left eye.

Left Eye A strand of vitreous extended from the pupillary area slightly upward and outward to the corneal incision. The lower part and the nasal side of the anterior chamber was free of vitreous. Atropine was discontinued, and 2 per cent pilocarpine nitrate was substituted.

February 18—Tension was 38 mm. in the right eye and 17 mm. in the left eye.

Left Eye Vitreous still protruded through the pupil, partially blocking it. Some vitreous presented in one of the transfixion holes in the iris.

Right Eye The eye was hard to palpation, with much exfoliation, steamy cornea, shallow anterior chamber, moderate conjunctival injection and mature cataract. With treatment with 4 per cent pilocarpine nitrate, the tension in the right eye dropped, varying from 15 to 26 mm. until February 26.

February 26—An intracapsular cataract extraction with basal iridectomy was done on the right eye. There was no loss of vitreous, but the anterior chamber formed while the patient was still on the table. Postoperatively there was pronounced iridocyclitis with membrane formation, the patient was treated with atropine. He was discharged on March 9.

March 25—**Right Eye** There was slight ciliary injection, the eye was soft, there were a pupillary membrane and many opacities in the vitreous. The patient was using atropine.

Left Eye Tension was 30 mm., the patient was using pilocarpine. The same amount of vitreous was present in the anterior chamber.

April 8—**Right Eye** Tension was 14 mm. The sutures were removed. There was still a moderate mixed injection. The anterior chamber was deep. The pupil was drawn up. There was a fairly dense pupillary membrane, with a red reflex. Some folds were present in the cornea, there were no cells in the anterior chamber.

Left Eye Tension was 27 mm. The eye was white and quiet. A strand of vitreous extended from the pupil to the lower end of the corneal incision. The anterior chamber was deep. The disk was nearly white.

Treatment The right eye was treated with heat four times a day, the left eye was given pilocarpine nitrate, 4 per cent, four times a day

April 22—Tension was 34 mm in the right eye and 20 mm in the left eye Examination showed no change in the left eye **Right Eye** The anterior chamber was shallow, especially above, a vascularized deep corneal opacity was present up and temporally from 8 to 1 o'clock, extending 2 mm into the cornea A dense pupillary membrane was present The remains of a few small keratic precipitates were seen on the lower half of the cornea There was slight epithelial edema of the upper third of the cornea There were no cells in the anterior chamber and no aqueous flare An emergency admission was advised but was refused by the patient

April 29—The patient was admitted to the hospital **Right Eye** Vision was limited to perception of hand movements The anterior chamber was shallow, there were no cells, but many old pigmented keratic precipitates were present The coloboma of the iris was filled with dense membrane The fundus was not seen Tension was 30 mm

Left Eye Examination showed no change Tension was 21 mm Vision was limited to counting of fingers at 4 feet (120 cm) The disk showed shallow cupping

April 30—Operation was performed on the right eye A double transfixion of the iris was done below There was a little bleeding of the iris, and the anterior chamber deepened slightly

May 2—The patient was discharged Vision with glass was 1/200 in the right eye and 20/100 in the left eye

May 6—Tension was 14 mm in the right eye and 25 mm in the left eye The patient had not been using drops in the left eye Medication was started again with 4 per cent pilocarpine nitrate, given four times a day

Right Eye The anterior chamber was deep The transfixion holes were barely visible

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ABSTRACT OF DISCUSSION

DR JOHN H DUNNINGTON, New York This timely paper focuses attention on some of the factors responsible for glaucoma in the aphakic eye By so doing, the authors have made a noteworthy contribution and, consciously or unconsciously, have entered a plea for a more detailed preoperative study of each patient They recognize that individualization in the treatment of these patients is essential Such a clearcut analysis of the causative factors and the rationale for different methods of relief should make all ophthalmologists conscious of the futility of adopting one operative procedure as a routine measure in all cases of this condition

In cases of type 1 the authors point out that the communication between the anterior and the posterior chamber may become blocked by a membrane, and they cite 3 cases in which this condition resulted in increased intraocular tension, relief being obtained by a discission in 2 of them They caution against the use of this operative procedure in the presence of normal vitreous—an opinion in which I heartily concur, for in my experience the cutting of a secondary membrane in the presence of an increased intraocular tension usually leads to aggravation of the preexisting glaucoma Considering the difficulty of determining the

exact status of the vitreous behind a dense membrane, the establishment of a communication between the anterior and the posterior chamber as an initial step is a safer operative procedure

Herniation of the vitreous through the pupillary area does not of itself produce glaucoma. As pointed out by the authors, it occurs only when the communication between the anterior and the posterior chamber is blocked, a condition not infrequently seen after a discission. Such blocking adhesions between the iris and the prolapsed vitreous occur more readily in the presence of a postoperative iridocyclitis, the frequency of which is in direct proportion to the amount of operative trauma. For this reason, I have long contended that a discission is not a minor surgical procedure, but one that should be done with the greatest care and with minimal disturbance of the vitreous. To relegate this operation to the novice is to increase the frequency of postoperative glaucoma. A careful preoperative study of the membrane will disclose how a satisfactory opening can be made in it with the smallest amount of trauma. The frequency of this type of glaucoma can be reduced materially by remembering that a small opening in a secondary membrane, if placed in the proper position, gives the same visual result as a wide one. Above all, unnecessary disturbance of the vitreous should be avoided.

The occurrence of glaucoma from herniation forward of the vitreous into the anterior chamber has occurred in several of my cases of intracapsular extraction, both with and without complete iridectomy. In most of them convalescence was complicated by a low grade cyclitis, which was followed in a short time by a rise in the intraocular tension. In these cases I have always recommended a cyclodialysis with iridectomy, as described by Wheeler in 1936, as the operation of choice. In view of the authors' findings, I believe that either a transfixion of the iris or an iridectomy should be considered, for I have long observed that a cyclodialysis, unless combined with an iridectomy, is ineffective in many cases of glaucoma with aphakia.

Herniation of the vitreous forward, blocking the communication between the anterior and the posterior chamber, may be the cause of the rise in tension that follows a delayed restoration of the anterior chamber. In 1 case of this type a restoration of normal intraocular tension followed the freeing of an adhesion between the anterior face of the prolapsed vitreous and the posterior surface of the cornea, whereas a previous cyclodialysis had failed to reduce the tension.

In some instances the increased tension resulting from a herniation of vitreous through the round pupil can be relieved by medical means. Restoration of the mobility of the iris by first dilating and then contracting the pupil was sufficient to control the tension in 2 of my cases. Let me emphasize the importance of detailed examination with the slit lamp as a part of the postoperative follow-up in cases of cataract extraction, particularly those with a round pupil. Such a herniation of the vitreous can be easily seen, and if it is associated with an immobile iris, beware! Similarly, the early detection of adhesions between the iris and the nonprolapsed (anterior) face of the vitreous should enable one to prevent the development of glaucoma from that cause. The failure of the authors to find any reference in the literature to cases of this sort is but proof that sufficient attention has not been given to the mobility of the iris.

Their case reports clearly demonstrate that a blockage of the pupil by vitreous may be responsible for glaucoma in some patients with a dislocated lens, and their method of treatment warrants serious consideration. My experience with cases of this type has been confined to the removal of the lens combined with a complete iridectomy, but, thanks to the authors, henceforth I shall always bear in mind that vitreous block is a factor to be reckoned with.

• DR PAUL A CHANDLER, Boston. Of all the types of glaucoma I have treated, this affords the greatest satisfaction to the surgeon. If a proper communication is reestablished between the chambers, so far as our present experience goes with the 14 cases discussed in this paper and with 3 or 4 others which are not included here, the results are uniformly successful. In case 8, in the second group, in which glaucoma came on after a needling, a simple puncture of the iris was done. A single dressing was applied, the patient was sent directly home and made a rapid and uneventful recovery.

A large herniation of the vitreous into the anterior chamber may occur without a pupillary block, and it is rare that the entire pupil is blocked with vitreous if a complete iridectomy has been done. It is known that there is a continuous exchange of fluid between the vitreous and the aqueous all the time, probably in these cases there is a little leakage of aqueous between the pupillary border and the herniating vitreous, but it is apparently not sufficient to make free communication between the chambers. The most dramatic proof to my mind that the vitreous can block the pupil is that when a communication is reestablished between the chambers one can see the vitreous withdraw from the anterior chamber.

Dr. Dunnington referred to the use of drops. If the pupil is blocked with vitreous, the drug of choice is atropine, instead of pilocarpine. Pilocarpine makes the condition worse, as was proved in several of our cases, because it makes the pupil grip the herniating vitreous all the more firmly and increases the degree of pupillary block.

MINOR ANOMALIES IN POSITION OF THE EYELASHES

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CILIUM INCARNATUM INTERNUM

THE SUBCUTANEOUS growth of an eyelash is infrequently reported. Makrocki¹ described the case of a woman aged 22 with two small nodules in each upper lid which proved to be eyelashes 3 to 4 mm in length. Except for unusually heavy pigmentation, they were normal. Herzog² described the case of a woman aged 24 with a wart the size of a pinhead on the outer margin of the left upper lid. On the inner circumference of the base of the wart a cilium was bent backward and grew along the margin of the lid, completely surrounded with epithelium. Slitting of the epithelium permitted the liberation of a normal eyelash to its normal position. Chernow³ mentioned as *Bedeutungsvolles Kinosum* a case in which a normally formed, extremely thick eyelash 8 mm long was found under the skin of the lid. Schreiber⁴ observed a 17 year old girl with a comblike vertical elevation of the skin immediately above the margin of the lid, completely surrounding an eyelash. Jess⁵ described the case of a 19 year old patient with a longitudinal swelling of the skin of the upper lid through which a cilium could be seen as a black stripe growing upward.

I observed a similar case, that of a man aged 39 who consulted me because he had difficulty in removing a blackhead from his left upper lid. Two millimeters nasal to the midline the left upper lid showed a longitudinal elevation of darker color than the surrounding skin. Examination with the slit lamp showed a cilium completely surrounded with epithelium. After a small incision with a Graefe knife near the margin of the lid, the cilium, 7 mm long, could easily be extracted with forceps. Apparently normal in all respects, it joined the patient's normal row of lashes. There was no other pathologic condition of the eyes (figure, A).

From the service of Dr. E. B. Gresser, Department of Ophthalmology, Beth Israel Hospital.

1 Makrocki, F. Ein Fall von pervers gewachsenen subcutanen Cilien, Zentralbl f prakt Augenh 7 129, 1883.

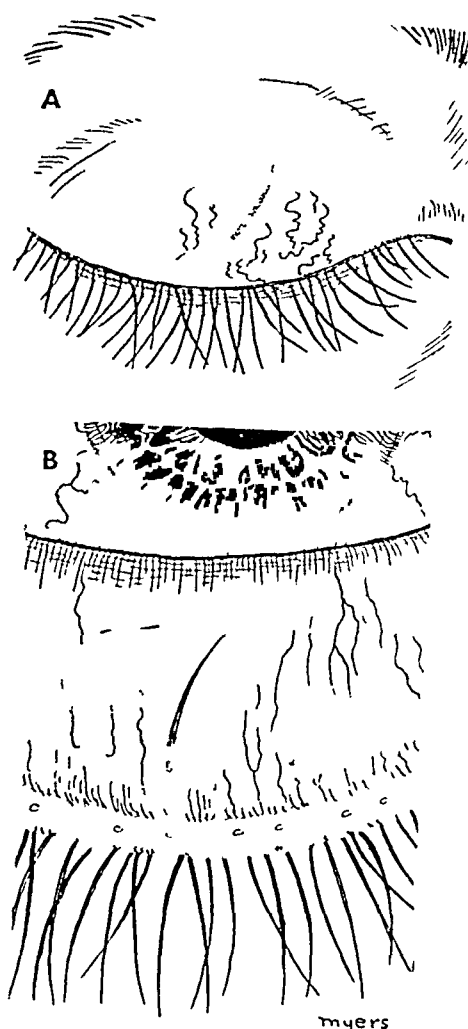
2 Herzog, H. Pathologie der Cilien, Ztschr f Augenh 12 256, 1904.

3 Chernow, F. Ueber die unter dem Namen Blepharitis ciliaris bekannten Erkrankungen des Lidrandes, Ztschr f Augenh 18 1, 1907.

4 Schreiber, L. Die Krankheiten der Augenlider, Berlin, Julius Springer, 1924, p 380.

5 Jess, A. Cilia incarnata totalis, Klin Monatsbl f Augenh 83 47, 1929.

Comment—This anomaly may have little practical importance, but the apparent rarity and the fact that no case has been published in the Anglo-American literature may justify its report. For the explanation of the condition it is not necessary to go into a far-fetched embryologic discussion, as Makröck¹ did. The sprouting eyelash encounters resistance, such as a wart or a large infarct of a meibomian gland, in



Artist's sketches of (A) cilium incarnatum externum and (B) cilium incarnatum internum

its growth. On being bent upward, it follows the line of least resistance finding its way under the skin of the lid.

CILIUM INCARNATUM INTERNUM

Cilium incarnatum internum is a rarer condition than the preceding one. In this form an aberrant cilium finds its way through the conjunctiva tarsi and is much more unpleasant to the patient. Eisner⁶ observed a 50 year old farmer who complained of a stinging pain in his right

⁶ Eisner, F. Beitrag zur Anomalie des Zilienwachstums, Klin Monatsbl f Augenh 85 810, 1930

eye for a few days. There was an erosion of the lower part of the cornea, caused by the tip of an eyelash which perforated the conjunctiva 1.5 mm below the margin of the lid. The cilium was easily removed, but it kept on growing back in this anomalous position and had to be removed again twice in the course of three years. Hirose and Hirayama⁷ reported a similar case, that of a 17 year old girl, in which a black hair was directed upward in the tarsal conjunctiva of the upper lid. The hair was found to be an eyelash.

I observed a similar case in a man aged 50 whose eyes had been normal at a previous examination. He complained that he had felt a scratching sensation in his right eye for the previous two weeks. The eye became increasingly red. Examination showed moderate injection of the lower part of the conjunctiva bulbi. The corneal surface was not as brilliant as normal but did not stain. After removal of mucus from the conjunctiva first, examination with the slit lamp showed a hair 2 mm below the margin of the lid in the midline. It was visible about 1.5 mm below the conjunctiva, and an end of the same size was moving freely in the cul-de-sac. A light pull with the forceps extracted the hair, which proved to be an eyelash, rather thin, little pigmented and slightly curled at its end. Two days later the patient presented himself as cured (figure, B).

Comment—The ingrowth of an eyelash and its appearance in the conjunctiva can be explained on a strictly mechanical basis, in the same way as cilium incarnatum externum. Before perforating the lid margin, the cilium, meeting an obstacle, is bent backward and enters by chance the lumen of a meibomian gland. It grows backward along the gland until it perforates the tarsus and the conjunctiva. However, there is a possibility that one is dealing with a congenital false hair anlage in which the root of the cilium faces the margin of the lid. Such a condition is known as *cilium inversum*, and a histologic specimen has been reproduced by Schreiber.⁸

SUMMARY

Two cases of anomalous upward growth of an eyelash are described. In the first case the cilium found its way into the outer skin of the lid, in the second case it perforated the conjunctiva, and its tip moved freely in the cul-de-sac.

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⁷ Hirose, K., and Hirayama, M. An Anomaly of the Eyelashes, Acta Jap Ophth Soc 3 108, 1932, abstracted, Arch Ophth 10 681 (Nov.) 1933

⁸ Schreiber,⁴ p 381

Clinical Notes

LATENT NYSTAGMUS FOLLOWING HEAD INJURY

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IN ORDER to find a satisfactory explanation for the signs and symptoms observed in a case of latent nystagmus, the literature on the subject has been surveyed and has been found not only wanting but with many contradictions. Kestenbaum¹ stated that the mechanism and genesis of latent nystagmus are still controversial and indefinite, while Duke-Elder² called the explanations of various authors quite hypothetical. According to Esters,³ the cause of the phenomenon is unknown. The purpose of this report is not to offer another theory to the many already advanced but, rather, to attempt to integrate and coordinate them for a better understanding of this interesting phenomenon, exemplified by a case following head injury.

There seems to be no doubt that latent nystagmus is a disturbance or perversion of the normal mechanism of extraocular muscle tonus, fixation and conjugate ocular movements. It is equally evident that, while many of their phases have been well worked out, there remain some controversial points difficult of experimental proof. There is definite evidence that the movements in latent nystagmus are conjugate and bilateral, and it appears in the light of present concepts that they must primarily be controlled from a coordinating center, wherever and whatever that is. While a supranuclear center for normal conjugate movements is generally accepted, such a center for latent nystagmus has been called by various names, such as "main ocular muscle sender," by Ohm⁴, "association centers," by Fuchs⁵, "lower centers," by Posner⁶, "coordinating cen-

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1 Kestenbaum, A. Clinical Methods of Neuro-Ophthalmologic Examination, New York, Grune & Stratton, Inc., 1946, p. 230

2 Duke-Elder, W. S. Text-Book of Ophthalmology, London, Henry Kimpton, 1942, vol. 1, p. 638

3 Esters, cited by Duke-Elder²

4 Ohm, cited by Kestenbaum, A. Physiological and Clinical Aspects of Nystagmus, in Ridley, F., and Sorsby, A. Modern Trends of Ophthalmology, London, Butterworth & Co., Ltd., 1940, pp. 372-381

5 Fuchs, E. Textbook of Ophthalmology, ed. 5, edited by A. Duane, Philadelphia, J. B. Lippincott Company, 1907, pp. 800-801

6 Posner, A. A Contribution to the Theory of Binocular Vision Supported by Three Cases of Latent Nystagmus, Am. J. Ophth. 28 392-396 (April) 1945

ters,' by Fromaget⁷, "supranuclear center," by Verhage,⁸ and "center of rhythmic coordination," by Rea.⁹ Bielschowsky's¹⁰ "anomalous innervation centers" is probably related to it. Whether this center is single, bilateral or multiple, the terms refer to the same thing physiologically. Wherever it is anatomically, whether in Deiters' nucleus, according to Ohm¹, in the quadrigeminal bodies, according to Whitnall,¹¹ or elsewhere in the mesencephalon, it must be connected directly or indirectly with the common motor pathways of the third, fourth and sixth nerves to the ocular muscles and with the many reflex peripheral sensory pathways, such as those from the labyrinth and the pathways mediating proprioceptive impulses from the muscles of the neck, light impulses from the retina and accommodation, convergence and fusion impulses, as well as the involuntary central impulses or innervations from the occipital lobes and the cerebellum and the voluntary innervation from the frontal lobes.

Many believe with Duane¹² that the act of fixation is influenced simultaneously under normal conditions by the left and the right frontal as well as the occipital cerebral motor centers. When the eyes are in the primary position, the right and the left centers exert equal innervations but when looking to the side, as to the right, the innervations, whether voluntary or reflex, although bilateral, are mainly from the left or opposite side, and vice versa. These central innervations are thought of as inhibitory and steadying (Posner⁶), or as actually stimulating to the impulses from the lower centers.

What is obscure, however, is whether these supranuclear lower centers are not generators, or the source of innervations of their own (Posner,⁶ Ohm¹) as well as coordinators. If they are not generators, then the extraocular muscle tone present after cerebral influence is removed must be from constant tonic innervations from the cerebellum or from proprioceptive impulses from the extraocular muscles through the third, fourth and sixth nerves (Sherrington¹³).

It is evident from this discussion that, while much depends on the congenital or acquired integrity or capacity of the coordinating mecha-

7 Fromaget, cited by Duke-Elder.²

8 Verhage, J. W. Eine klinische Studie über den Nystagmus latens, *Ophthalmologica* **103** 209-224 (April) 1942.

9 Rea, L. R. *Neuro-Ophthalmology*, St. Louis, C. V. Mosby Company, 1938, pp. 65-73.

10 Bielschowsky, A. *Lectures on Motor Anomalies*, Hanover, N. H., Dartmouth College Publications, 1943, p. 19.

11 Whitnall, cited by Rea,⁹ p. 117.

12 Duane, A. The Associated Movements of the Eyes, Their Nerve Centers Conducting Paths, Production, Varieties and Derangements, *Am. J. Ophthalm.* **3** 16-26 (Jan.) 1924.

13 Sherrington, cited by Duke-Elder,² p. 579.

nism, its workings and the impulses coming from it to the common motor pathways may be influenced quantitatively and qualitatively for smooth or perverted ocular movements by any one or more normal or abnormal impulses reaching it from any direction. Failure to recognize this may give rise to various concepts of the etiology and mechanism of latent nystagmus, such as disturbance of the coordinating centers (Fuchs⁵ and Fromaget⁷), inhibition of convergence (Roelofs¹⁴), labyrinthine disturbance and difference in light tonus (Ohm⁴), congenital lability of the optical apparatus with disturbance of the balance between the right-sided and the left-sided stimulation in the supranuclear centers (Verhage⁵) and presence or absence of sharp images on the macula lutea (Kestenbaum¹)

REPORT OF A CASE

A man aged 24, a Filipino veteran of Bataan, was first seen on Aug 12, 1942, with complaints of blurring of vision, headache and dizziness. About eight months before, while in action, he sustained an injury to the left occipitoparietal area from fragments of an artillery shell. He was unconscious for many hours and lost much blood. Since a week after he was injured he had noted difficulty in fixing his gaze on objects, which seemed to him to move jerkily from side to side, accompanied with horizontal movements of both eyes, especially the right. On persisting in fixating, he experienced a sensation of instability and frontal, and sometimes occipitoparietal, headache. There was no rotatory vertigo or deafness. He had had no ocular complaints before this head injury. He had malaria and dysentery while a prisoner of war in Capas, but no venereal infection. There had been slight subjective improvement since the onset of his complaints.

He appeared fairly well nourished. There were a thick linear scar, about 4 inches (10 cm) long, in the left occipitoparietal region and a superficial scar back of the left pinna. There was slight intermittent exotropia, with the right eye usually deviating, this disappeared, especially on fixation for near objects. With the eyes in the primary position for far vision there was no definite gross nystagmus. With the eyes right, spontaneous, transient, jerky horizontal nystagmus of both eyes to the right was present. With eyes left, a similar nystagmus, of lesser intensity, was noted. When the eyes were in the primary position and the left eye was covered, pronounced jerky nystagmus of both eyes would appear, which increased in amplitude and frequency as the eyes were turned to the right but disappeared as the gaze was turned to the left. If the right eye was covered, a similar, less intense, nystagmus appeared, but only on looking to the left. In the dark room, pronounced nystagmus could be elicited by directing the ophthalmoscopic light on the right macula, but not by directing the beam on the other regions of the fundus of the right eye or on the macula of the left eye. No limitation of movement, diplopia or vertical nystagmus was present.

The pupils showed no abnormality. The near point of convergence was 10.5 cm. Far vision was 20/60 in the right eye, with the head turned slightly to the right, it was 20/30 in the left eye and was 20/25 with a correction of 0.62 D sph. With both eyes fixing, far vision was 20/25, and near vision was ability to read Jaeger type 1. Accommodation was 8.00 D in the right eye and 8.50 in the left eye. The patient could not sustain reading after a few minutes. Binocular vision

14 Roelofs, cited by Duke-Elder²

was present, as shown by bar reading, the Cruise stereoscope and the Lancaster red-green test. Third degree fusion was present. Its amplitude was not taken. Except for slight pallor of the disk, the fundus was normal on each side. Examination of the visual fields (Ferree-Rand perimeter) showed slight contraction in the left eye, while the field in the right eye could not be accurately taken. With the stereocampimeter the right field was equal to the left, without any hemianopsia. The blindspot of the left eye was normal, while that of the right eye could be mapped out only inaccurately. No scotoma was present on either side.

Hearing in the tuning fork test was practically normal on both sides. Vestibular tests for the horizontal canals gave the following results. Nystagmus was produced in twenty-two seconds when the cold caloric test was performed on the left side and only after thirty-two seconds when it was done on the right side, but in the turning test there was longer after-nystagmus on turning to the left (sixty-two seconds) than on turning to the right (forty-two seconds). The Romberg test was performed with slight swaying. There was no spontaneous past pointing.

The neurologic impression reported (Dr M. Lunson) was purpuric, post-traumatic hemorrhages, meningeal, cortical and intracerebral, especially in the fronto-occipital region and the mesencephalon. Moderate malarial splenomegaly was present. The blood showed malarial parasites but was otherwise normal. The blood pressure was normal. A roentgenogram of the skull showed no fracture. The Wassermann reaction of the blood was 2 plus. The spinal fluid was under normal pressure, with normal cytologic and chemical constituents.

The patient was followed for over six months, he showed slight improvement in headache, dizziness and reading ability, but objectively the latent nystagmus was practically unchanged.

COMMENT

A single 2 plus Wassermann reaction of the blood with a normal spinal fluid, a history of malarial infection and a negative history for venereal disease is of no account. Although the hearing was normal, the caloric test showed vestibular hyposensitivity, but the rotatory test revealed a stronger or longer state of instability on the right side. This is peculiar, indicating a perverted reaction or an unstable state of the vestibular nuclei (Deiters), and may influence both the production of the transient end nystagmus with both eyes open and the character of the nystagmus with one eye closed. The lower coordinating centers appear to be in the region of Deiters nucleus, in the mesencephalon. But a far stronger influence for the production of the latent nystagmus in this case was the perverted state and function of the higher involuntary ocular motor centers, especially the left occipital lobe, accounting for the appearance of nystagmus when one eye, especially the left, was closed during reflex stimulation by monocular images or strong light. A similar state of unbalanced dysfunction of the voluntary ocular motor centers in the frontal cortex, especially the left, may help explain the difference in intensities of the latent nystagmus with the eyes in the primary position and that elicited with the lateral directions of gaze.

The thesis of this communication is that the peripheral sensory stimuli and the state of stability of the lower coordinating centers, as

well as the balance of the innervating influence of the higher voluntary and involuntary centers, must be considered as a whole in the explanation of the mechanism of latent nystagmus, and probably of all nystagmus. In the case reported, this perverted condition of the higher and lower centers seemed to have followed severe concussion of the brain in a constitution debilitated by malaria, malnutrition and nervous exhaustion brought about by the war. There may, however, have been a congenital or inherent lability of the central nervous system as in most cases of latent nystagmus reported.

TREATMENT OF CORNEAL ULCER WITH BLOOD AND BLOOD PLASMA

ERWIN E. GROSSMANN, M.D., MILWAUKEE

IT IS notable that the cornea is avascular and derives its nourishment by dialysis from the perilimbal plexus. For this reason healing of corneal infections may become sluggish and prolonged. It is also notable that frequently lesions of the cornea clear up only after vascularization has occurred. According to Duke-Elder,¹ the neovascularization is a response to a call for help by a tissue in difficulty.

In view of the lack of an adequate nutrient supply system in the cornea, it would appear logical to apply the needed nutrient elements directly to the cornea in the form of drops, made up either of whole blood or of blood plasma. Although, so far as is known, this procedure has never been reported as an adjuvant in the treatment of corneal ulcer, excellent results have been reported by other workers from its use in local treatment of ulcers of the leg.

Murray and Shaar² reported gratifying results when blood was used in paste form in several cases of indolent decubitus ulcers and in infected wounds. Moorhead and Unger³ and his associates reported similar excellent results using a red blood cell concentrate.

Naide⁴ used blood and concentrated blood plasma with good results in the treatment of ulcers of the leg.

Many ophthalmologists will attest to the fact that in spite of the advent of sulfonamide drugs and other antibiotics many corneal diseases still resist either one or both of these excellent remedies. I have seen instances of epithelial erosion in degenerated phthisical eyes. I sincerely

1 Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1938, vol. 3, p. 1840.

2 Murray, C. K., and Shaar, C. M. Red Blood Cell Paste in the Treatment of Ulcers and Chronically Infected Wounds, *J. A. M. A.* **125** 779-782 (July 15) 1944.

3 Moorhead, J. J., and Unger, L. J. Human Red Cell Concentrate for Surgical Dressings, *Am. J. Surg.* **59** 104-105 (Jan.) 1943.

4 Naide, M. Treatment of Leg Ulcers with Blood and Concentrated Plasma, *Am. J. M. Sc.* **205** 489-493 (April) 1943.

doubt whether these recurrent staining lesions are ever manifestations of bacterial disease. These erosions are more likely due to an impoverished corneal tissue made less permeable to dialysis by the degenerated tissue.

An attempt was made to evaluate the use of whole blood and blood plasma in the treatment of corneal diseases. Six cases are briefly described.

REPORT OF CASES

CASE 1—A man aged 23 brushed against a twig in the dark, resulting in an epithelial abrasion, measuring 3 mm, of the right cornea. Treatment consisted of atropinization and application of hot compresses and sulfathiazole ointment. After four days of this regimen, the lesion still stained well, the globe remained injected and the lesion showed beginning leukocytic infiltration. Pooled human blood plasma was then used in the form of drops every three hours. In forty-eight hours the lesion failed to stain. Recovery was complete without scarring.

CASE 2—The patient, aged 24, also received an epithelial abrasion of the cornea from walking into a low-hanging branch in the dark. When, at the end of four days, the customary treatment had failed, blood plasma was used, as in the preceding case. Healing occurred in forty-eight hours.

CASE 3—A man aged 28 had a lesion of the left eye diagnosed as dendritic keratitis. Treatment consisted of daily applications of half-strength tincture of iodine, atropinization and heat. At the end of ten days the lesion appeared to be spreading. In this case blood was drawn from the antecubital vein and dropped immediately directly onto the cornea. A bandage was then applied. This procedure was repeated daily for six days, when only slight staining could be noted. There was no further spread of the lesion.

CASE 4—A man aged 30 was seen on several occasions because of recurrent ulcerations in a blind eye manifesting bandlike keratitis. The lesions appeared in dotlike fashion, with frequent coalescence, on the surface of the degenerated cornea. Penicillin and sulfathiazole applied locally failed to remedy the situation. Whole blood was again used, as in case 3, and healing occurred within four days.

CASE 5—A man aged 52, known to be alcoholic, had an area of denudation involving the lower half of the cornea. The upper border of the lesion showed a yellowish gray infiltration. The general appearance was that of beginning serpiginous ulcer. Whole blood was dropped daily onto the eye, which was then bandaged. Within seven days the lesion healed, leaving no opacities.

CASE 6—A soldier, aged 42, received a trivial abrasion of the cornea while on duty in England. According to the report by his attending physician (I did not see the patient),⁵ the lesion developed into a serpiginous ulcer and became intractable to all forms of treatment. Whole blood was used as a local application several times a day, in addition to the usual routine of atropinization, application of heat, fever therapy, and administration of sulfathiazole and penicillin. The lesion began to show signs of improvement within seventy-two hours, and complete recovery ensued.

CONCLUSIONS

It is obvious that these 6 cases hardly substantiate a definite conclusion regarding the value of blood in the treatment of corneal ulcer. It

5 Shure, I. Personal communication to the author.

would seem, however, that its use is physiologically sound, and beneficial results have been obtained. The small series of cases does not permit one to choose between the use of whole blood and that of blood plasma. It would appear, however, that the whole blood is preferable. For one thing, whole blood is always conveniently available from the patient. Furthermore, when whole blood is dropped slowly in single drops on the eye, it tends to collect and partly coagulate in the fornices, so that prolonged contact is assured. The application of a bandage further enhances the prolongation of contact.

238 West Wisconsin Avenue

News and Notes

EDITED BY DR W L BENEDICT

UNIVERSITY NEWS

Postgraduate Course in Ophthalmology, Medical Extension, University of California Medical School—Announcement is made of the postgraduate course in ophthalmology to be given by the University of California Medical School, Medical Extension, Sept 15 to 19, inclusive, 1947, daily from 8 30 a m to 12 noon and from 1 30 to 5 p m

Requests for information and for registration are to be addressed to Dr Stacy R Mettler, head of Postgraduate Instruction, Medical Extension, University of California Medical Center, San Francisco 22

Graduate Course in Ophthalmology of the University of Rochester School of Medicine—The fifteenth summer graduate course in ophthalmology of the University of Rochester School of Medicine will be held in Rochester, N Y, on July 28, 29, 30 and 31, 1947. The program will be as follows:

July 28 "Nystagmus, a Clinical Classification," C Wilbur Rucker, M D, "Oblique Muscle Surgery," John M McLean, M D, "Use of Vasodilators in Ophthalmology," Walter F Duggan, M D, "Lesions of the Optic Chiasm," C Wilbur Rucker, M D, "The Cataract Operation," John M McLean, M D, "Tangent Screen Scotometry," Walter F Duggan, M D, "Classifications of Systemic Hypertensive Vascular Diseases," F L Philip Koch, M D

July 29 "Misconceptions in Neuro-Ophthalmology," P J Lempfelder, M D, "Early Glaucoma," Hendrie W Grant, M D, "Slit Lamp Biomicroscopy," Milton L Berliner, M D, "Etiologic Factors in Retinal Hemorrhages," P J Lempfelder, M D, "Divergent Strabismus," Hendrie W Grant, M D

July 30 "Disopropyl Fluorophosphate, a New Miotic," Edwin B Dunphy, M D, "Ocular Therapeutics in the Office," Parker Heath, M D, "Orthoptics," LeGrand H Hardy, M D, "Headaches and Ocular Pain," Edwin B Dunphy, M D, "Color Vision Tests," LeGrand H Hardy, M D, "Ocular Therapeutics in the Hospital," Parker Heath, M D

July 31 Visits to the surgical clinic, Strong Memorial Hospital, and the Bausch & Lomb factory

Applications should be made to John F Gipner, M D, Strong Memorial Hospital, Rochester 7, N Y. The registration fee is \$15, the matriculation fee, \$25.

SOCIETY NEWS

Wilmer Residents Association—The sixth clinical meeting of the Wilmer Residents Association was held at the Wilmer Ophthalmological Institute, the Johns Hopkins Hospital and University, on April 17 to 19, 1947. It was a successful meeting, with an attendance of 235.

The meeting began with a joint conference in conjunction with the department of medicine on "Sarcoidosis," led by Dr McGee Harvey, Dr A Murray Fisher and Dr Alan C Woods, and "The Progress of Arteriolai Disease," led by Dr James Boidley and Dr Jonas S. Friedenwald. The purely ophthalmologic papers then followed: "Ocular Effects of Triiodine," Dr Louise Sloan, "Retrolental Fibroplasia," Dr William C Owens, "Roentgen Irradiation in the Treatment of Ocular Diseases Characterized by New-Formed Blood Vessels," Dr Jack S Guyton and Dr Algernon B Reese, "Experimental Study of Corneal Transplants," Dr Alfred E Maumenee, "Surgical Treatment of Paralytic Inferior Oblique," Dr John M McLean, "Conference on Clinical Pathology," Dr Russell T Snip and Dr Jonas S Friedenwald, "Cystic Malignant Melanoma of Uvea," Dr Robert E Kennedy, "Role of Rutin and Anticoagulants (Dicumarol) in Treatment of Retinal Vascular Disease," Dr Angus L MacLean, "Tantalum Implant for Glaucoma," Dr Malcolm W Bick, "A Fixation Light for Testing the Six Cardinal Positions of the Eye," Dr William C Owens, "Studies of the Physiology, Biochemistry and Cytopathology of the Cornea in Relation to Injury by Mustard Gas [dichloroethyl sulfide] and Allied Agents," Dr Jonas S Friedenwald, "Use of Anterior Chamber of the Eye in Cancer Research," Dr Albert C Snell Jr and Dr John Schilling; "Chemotherapy in Experimental Ocular Tuberculosis," Dr Alan C Woods, "Injection of Saline Solution into the Eye in Operations for Retinal Detachment," Dr Jack S Guyton, "Sympathetic Ophthalmia," Dr Samuel D McPherson, "Demonstration of a New Type Beta Ray Applicator," Dr Charles E Iliff, "Experimental Production of Dinitrophenol Cataract," Dr Wilhelm F Buschke, "New Types of Plastic Implants After Enucleation," Dr Russell T Snip, "The Oculocardiac Syndrome Differential Diagnosis," Dr Frank B Walsh; "Use of Diisopropyl Fluorophosphate (DFP) for Glaucoma," Dr William G Marr, "Use of Furmethide [Furfuryl Trimethyl] for Glaucoma," Dr Ella Uhler Owens, "Apparatus for Chromatic Stimulation of Single Nerve Fibers of Mammalian Retina Demonstration of Corneal Potential," Dr Samuel A Talbot and Dr Stephen W. Kuffler.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society—The Louisiana-Mississippi Ophthalmological & Otolaryngological Society held its annual meeting at the Buena Vista Hotel, Biloxi, Miss, on May 5, 1947.

Dr George Adkins, of Jackson, Miss, president of the society, presided over the meetings. The following papers were presented: "The Rhinoplastic Operation and Restoration of Nasal Function," Dr Samuel Fomon, New York, "Newer Trends in Treatment of Ocular Diseases," Dr Peter C Kronfeld, Chicago, "Ménière's Disease," Dr Henry L Williams, Rochester, Minn, and "Allergic Problems Seen by the Ophthalmologist and Otolaryngologist," Dr Ralph Bowen, Houston, Texas.

Dr Noel Simmonds, of Alexandria, La, was elected president, and Dr Edley H Jones, of Vicksburg, Miss, was reelected secretary. The 1948 Convention will be held in New Orleans.

Central Illinois Society of Ophthalmology and Otolaryngology—The seventh meeting of the Central Illinois Society of Ophthalmology and Otolaryngology was held at the Hotel Lincoln-Douglas, Quincy, Ill., on April 26 and 27. The following ophthalmologic papers were presented: "Roentgen Therapy of Inflammatory Lesions About the Eye," Edward C. Albers, M.D., Champaign, Ill.; "Narrow Angle Glaucoma," "The Filtering Scar" and "Preparation and Preservation of Ophthalmic Solutions and Ointments," Peter C. Kronfeld, M.D., Chicago (by invitation).

Association for Research in Ophthalmology—The sixteenth scientific meeting of the Association for Research in Ophthalmology was held at Atlantic City, N. J., on June 10, 1947. The following papers were presented: "Bilateral Granulomatous Uveitis from the Use of Horse Serum in Rabbits," T. F. Schlaegel Jr., M.D., Indianapolis; "Stimulation of Corneal Epitheliation with Local Application of Erythrocytes," Frank W. Newell, M.D., Chicago; "Effect of Diisopropyl Fluorophosphate on the Capillaries of the Anterior Segment of the Eye," Ludwig von Sallmann, M.D., New York; "Transfer of Ascorbic Acid and Related Compounds Across the Blood-Aqueous Barrier," V. Everett Kinsey, Ph.D., Boston; "Acute Reversible Cataract in Chicken Due to Various Nitrocompounds," Wilhelm Buschke, M.D., Baltimore; "Virus Studies in Lymphomatoid Disease of the Ocular Adnexa," Alton E. Braley, M.D., and Rose Alexander, M.S., New York; "Cyanide Inhibition of Corneal Respiration," W. A. Robbie, Ph.D., P. J. Leinfelder, M.D., and T. D. Duane, M.D., Iowa City; "Ocular Effects of Trimethadione (Tudione)," Louise L. Sloan, Ph.D., and Anita Peck Gilger, M.D., Baltimore; "Reaction of Various Types of Fat Transplanted into the Orbit of Guinea Pigs Prior to the Development of Exophthalmos," George K. Smelser, Ph.D., New York; "Conjunctivitis with Membrane Formation," Michael J. Hogan, M.D., San Francisco; "Studies of the Physiology of the Eye Using Tracer Substances," Walter S. Wilde, Ph.D., Roy S. Scholtz, M.D., and Dean B. Cowie, Ph.D., Baltimore; "Pityrosporum Ovale in Seborrheic Blepharitis and Conjunctivitis," J. S. Gots, M.D., Philadelphia, Phillips Thygeson, M.D., San Francisco, and M. Waisman, M.D., Tampa, Fla.

Ophthalmological Society of the United Kingdom—The annual congress of the Ophthalmological Society of the United Kingdom was held in the department of zoology of the University of Glasgow, Scotland, on Thursday, Friday and Saturday, March 27, 28 and 29, 1947. The president was Dr. A. J. Ballantyne.

The following papers were read: "Induction of an Experimental Tumor of the Lens," Prof. Ida Mann; "An Unusual Form of Retinal Detachment (Cystic?) Seen in Children," M. F. A. Julei; "A Classification of Epiphora, with Comments on Diagnosis and Treatment," Dr. H. M. Traquair; "Some Aspects of Lid and Socket Repair," Mr. J. Scott Tough (introduced by the president); "Bilateral Retinal Detachment Associated with Choroidal Cyst: A Clinical and Pathologic Report," Dr. J. Pendleton White and Dr. I. C. Michaelson; "Corneal Blood Staining," Prof. A. Loewenstein; "Reiter's Disease," M. R.

Lindsay-Rea "Relation of Sjogren's Disease, Plummer-Vinson Syndrome and Ariboflavinosis," Dr E Godfredsen, "Holes at the Optic Disk" Mr H Neame, "Self-Inflicted Ocular Injuries," Dr L B Somerville-Large, "Vision During Glancing Movements of the Eyes," Dr G H Bell and Dr J B de V Weir (introduced by Prof W J B Riddell), "Vascular Disturbances in the Eye Following Concussion Injuries," Dr A M Wright Thomson, "Ocular Infections with *Cysticercus cellulosae*," Prof W H Melanowski, "Schnabel's Cavernous Atrophy," Mr Eugene Wolf, and "Some Aspects of Disease Affecting the Retinal Veins" Dr A J Ballantyne and Dr I C Michaelson. The address of the president was entitled "De Senectute"

The main topic consisted in a discussion of "Rhynology in Relation to Ophthalmology" Dr J Marshall, Mr G H Howells and Dr R McWhirter opened the discussion

On one afternoon there was a clinical meeting at the Glasgow Eye Infirmary. The annual dinner took place in the Hall of the Royal Faculty of Physicians and Surgeons on Thursday, March 27, and the other entertainments consisted in visits to a steel mill, to the Glasgow Art Galleries and to the Hunterian Museum

GENERAL NEWS

Dr. Parker Heath Appointed Pathologist at Massachusetts Eye and Ear Infirmary.—Dr Parker Heath, of Detroit, on July 1, 1947 will become pathologist at the Massachusetts Eye and Ear Infirmary, Boston. He will also be in charge of postgraduate teaching of ophthalmology at Harvard Medical School, with the rank of clinical professor

Stanford University Eye Bank—Officials of Stanford University have announced the establishment of an eye bank, to be located at Stanford University Hospitals, San Francisco. The eye bank, which is under the direction of Dr Dohmann K Pischel, will be similar to those now established in New York, Boston and Chicago. A bill now pending will, on passage, make it lawful to will eyes in the state of California

Institute of Ophthalmology, New York—The ninth annual meeting of the staff and alumni of the Institute of Ophthalmology, Presbyterian Hospital, New York, was held on May 2 and 3, 1947.

The program was as follows: "Primary Epithelial Tumors of the Ciliary Body," Dr Joseph Wadsworth, New York, "Achromatopsia—Report of a Case," Dr Louise Goux, Detroit, "Protein Derangement in Diabetes and its Effect on Diabetic Retinopathy," Dr G T Schwarz, Cleveland, "Virus Diseases of the Cornea," Dr A E Braley, New York, "Melanosis Oculi with Secondary Glaucoma," Dr F P Calhoun Jr, Atlanta, Ga., "The New Radiotherapy Department," Dr G Merriam and Dr Hayes E Martin, New York, "Technic of Muscle Surgery" (motion pictures), Dr Lloyd Morgan, Toronto, Canada, "Pigmented Tumors," Dr A G Reese, New York, "Reaction of Fat Transplantation into Orbit. Regeneration of Corneal Epithelium as Affected by Basal Metabolic Rate," Dr George K Smelser, New York, "Surgical Correction of Paresis of the Superior

Oblique Muscle," Dr W P McGuire, Winchester, Va , "Evaluation of Aniseikonia," Dr John P Macrie, New York , "Congenital Impatency of the Nasolacrimal Duct," Dr Dupont Guerry, Richmond, Va , "Recent Development in Color Vision Testing," Dr LeGrand H Hardy, New York , "Amblyopia from Cinchona Compounds," Dr H Rhodes, Pittsburgh , "Split Skin Graft to Cover Dura," Dr E B Hague, Buffalo, DFP [diisopropyl fluorophosphate]," Dr L Sallmann, New York , "Brawny Scleritis," Dr M Noel Stow, Washington, D C , "Chorioideremia," Dr Clement McCullough, Toronto, Canada

PERSONAL NEWS

Dr. Barkan Guest Speaker at Amsterdam Meeting—Dr Otto Barkan is leaving this week for the Netherlands, where he has been invited by the Netherlands Ophthalmological Society and the Society for the Prevention of Blindness to be the guest speaker at their annual meeting in Amsterdam on June 7 and 8 on the subject of "Glaucoma Operations"

Obituaries

WALTER IVAN LILLIE, M D

1891—1947

Walter Ivan Lillie was born in Grand Haven, Mich., on Nov 5, 1891. His untimely death followed acute dilatation of the heart, which was precipitated by his efforts to get his automobile out of a snowdrift while on his way to his office on the morning of Feb 21, 1947. His death, occurring without any warning to him or to his friends, was a great shock to all who knew him.

He received his degree of Doctor of Medicine from the University of Michigan in 1915 and was appointed a fellow in ophthalmology at the Mayo Clinic in 1917. He served as a member of the Medical Reserve Corps in the American and British Expeditionary Forces in the first World War. He received his degree of Master of Science in ophthalmology at the Mayo Clinic. In 1925 he became a consultant in ophthalmology, and shortly after that he was advanced to associate professor in the Graduate School of the University of Minnesota. In 1933 he was appointed professor of ophthalmology at Temple University School of Medicine, in Philadelphia, in which capacity he continued until his death.

Dr Lillie was a member of the American Medical Association, the American Academy of Ophthalmology and Oto-Laryngology, the American Ophthalmological Society, the American College of Surgeons, the College of Physicians of Philadelphia, the Harvey Cushing Society, the Sydenham Medical Coterie of Philadelphia, Sigma Xi and Phi Beta Pi medical fraternity. He was a past president of the Section of Ophthalmology of the Philadelphia County Medical Society and chairman of the society's Committee for the Conservation of Vision. He was a guest lecturer in neuro-ophthalmology at the Graduate School of Medicine of the University of Pennsylvania.

Dr Lillie possessed a charming and gracious personality that endeared him to his friends and colleagues. He had a keen sense of humor and an optimism which never deserted him even in adversity, and which was a source of solace to his friends and patients, who were devoted to him and had unlimited confidence in him. He was especially interested in the problems of the young men in medicine and gave much time to the betterment of his staff, residents and colleagues. He had a sound and brilliant mind and an unusual sense of fairness and honesty.

Dr Lillie's chief interest was neuro-ophthalmology. His diagnostic acumen, particularly in his field, was unusual. Unfortunately, a text-

book on neuro-ophthalmology which he was writing remains unfinished. He was a resourceful surgeon, who was at his best when the task was especially difficult. He was an outstanding teacher and contributed generously to the ophthalmologic literature.

Dr. Lillie was a remarkably successful departmental head, and he engendered an *esprit d'corps* among his staff, so that all worked enthusi-



WALTER IVAN LILLIE, M.D.
1891-1947

astically, cooperatively and cheerfully together in an atmosphere which was delightful. The devotion of each member of the department to their chief was complete.

The first half of Dr. Lillie's medical career was spent at the Mayo Clinic. While there, he won the friendship, admiration, confidence and respect of the entire staff. He was one of the outstanding consultants at Mayo Clinic. During the last half of his career he reorganized the

Department of Ophthalmology of Temple University School of Medicine and made it outstanding. He was an excellent consultant, always respecting the opinion of the referring ophthalmologist. Dr Lillie earned an outstanding place in American ophthalmology, where his work was appreciated, his opinion respected and his friendship cherished.

Dr Lillie's avocation was trap shooting, in which sport he won many trophies. He was twice champion of the Philadelphia Country Club in this sport.

Dr Lillie was fortunate in having as his life partner Opal Jones Lillie, who was a constant inspiration to him in his lifework. He is survived by his wife and son Robert. A son, Philip, of the Aviation Corps, met his death while in the service of his country in World War II.

In his death, the specialty of ophthalmology has lost one of its most illustrious members, and Philadelphia, one of its most valuable citizens, whose place cannot be adequately filled.

GLEN G GIBSON, M D

Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Anatomy and Embryology

ANATOMIC STUDY OF A COMPLEX RETROBULBAR EMBRYONIC MALFORMATION G OFFRET, *Arch d'ophth* 5:51, 1945

This study was prompted by observations at autopsy. The histologic study presented a complex malformation in the retrobulbar muscle cone characterized by fragments of malpighian epithelium, glands of the skin and glands of the salivary and mucous type. The author discusses tumors of this type occurring in this area according to the classification of Van Dujse: serous cyst, dermoid cyst and teratoma. Excellent photomicrographs accompany the article, and the author states the belief that the tissue which he has studied lies between a dermoid and a teratoma, since the histologic picture revealed such a multiplicity of different tissues.

S B MARLOW

Biochemistry

THE TRYPTOPHAN CONTENT OF THE LENS PROTEINS H SULLMANN, *Ophthalmologica* 108:281 (Dec) 1944

The tryptophan contents of the lens proteins of calf, cattle and pig eyes are given. The values were obtained by various methods from hydrolyzed and nonhydrolyzed lens proteins. The author's values are substantially greater than those found in the literature. He considers that most of the tryptophan is found in the beta crystalline form.

F H ADLER

Conjunctiva

CONJUNCTIVITIS ASSOCIATED WITH ERYTHEMA MULTIFORME BULLOSA, E E GROSSMANN, *Am J Ophth* 29:1146 (Sept) 1946

Grossmann reports 7 cases illustrating the association of conjunctivitis with erythema multiforme bullosum. This was apparently checked by sulfathiazole or penicillin therapy, these remedies acting as prophylactic rather than as curative substances.

W S REESE

CONJUNCTIVITIS CAUSED BY VIRUS OF NEWCASTLE DISEASE J A M A 132:169 (Sept 21) 1946

In October 1945 in Mikve Israel, a small agricultural settlement, an epidemic of 17 cases of conjunctivitis was reported by J Yatom. The infection almost exclusively attacked women who had contact with fowl affected with Newcastle disease. No direct spread from man to man was noted, and none of the women infected their husbands. After an incubation period of three days, swelling of the conjunctiva, tarsus and sclera developed without involving the cornea. After an acute stage of three days' duration characterized by a slightly mucous, purulent secre-

tion, the symptoms subsided within ten to fourteen days, with full recovery. In contrast to the conjunctivitis which is endemic in Palestine, the infection was characterized by being confined to one eye and by not involving the cornea. The epidemic stopped as soon as the affected fowl were slaughtered.

J A M A (W ZENTMAYER)

CONJUNCTIVAL FINDINGS IN CASES OF COLD HAEMAGGLUTINATION S
GORDUREN, Brit J Ophth 30:613 (Oct) 1946

Cooling the conjunctival sac was accomplished by using isotonic solution of sodium chloride in varying temperatures. The normal appearance of the blood column in the vessels at 37 C (98.6 F) began to disappear at this temperature, and at 27 C (80.6 F) the changes became obvious, blood corpuscles agglutinated in the vessels and divided into columns. This took place first in the superficial small vessels, with the decrease in temperature the same process occurred in the deeper vessels, where the blood columns were divided into sections with movements synchronous with systole. When examined with the biomicroscope, the segmented blood columns were irregular and had the appearance of a flocculated mass made of aggregated blood cells. Other changes are described as occurring with variations in temperature.

W ZENTMAYER

Cornea and Sclera

PENICILLIN AND VITAMIN C IN THE TREATMENT OF HYPOPYON ULCER
T C SUMMERS, Brit J Ophth 30:129 (March) 1946

Summers reports a series of cases of serpent (hypopyon) ulcer. The cases are divided into two classes: those in which the condition was regarded as hopeless from the start, and those in which there was a reasonable expectation of treatment producing a satisfactory result. In the desperate cases treatment was by phenolization of the ulcer, instillation of a solution of penicillin every hour during the day and every three hours during the night, use of atropine and hot pads, short wave diathermy and injection of a preparation of ascorbic acid. In the first group, of 3 cases, the ulcer healed in 1 case, but later a descemetocoele developed and the eye was enucleated. In the second group, of 9 cases, no eye was lost. The author is greatly impressed with the value of penicillin. If it is used over a long period the eye remains red, either as the result of the penicillin medication or from irritation due to nonpathogenic organisms. Curettement might be better than phenolization of the ulcer. Penicillin and ascorbic acid together produced a much quicker result than either alone.

A number of colored plates illustrate the article.

W ZENTMAYER

CORNEAL COMPLICATIONS FOLLOWING MALARIAL THERAPY M COR-
RADO, Ann ottal e clin ocul 72:22, 1946

Two cases of herpetic keratitis developing during the course of malarial fever therapy are described. The author proposes the administration of massive doses of thiamine hydrochloride in all cases selected for such treatment, purely as a measure for prevention of these corneal lesions.

G B BIETTI

FURTHER OBSERVATIONS ON KERATITIS PRODUCED BY ALCOHOL VAPOR
E ROMERO ROBLES, Arch Soc oftal hispano-am 4: 257 (April)
1945

This is the continuation of a previous report made in 1944 on this condition. Since then, the author has collected 20 more such cases. There is a characteristic corneal lesion which takes the stain poorly, and there is no clearcut delineation between the affected area and the normal epithelium, this being due to the fact that the damaged epithelium which has separated from the underlying tissues has not yet been shed.

The condition is brought about by exposure to ethyl alcohol vapor, and not directly to the alcohol itself. The symptoms are sudden violent pain, sensation of a foreign body, photophobia, blepharospasm, congestion, lacrimation and involvement of the iris without exudate, all without the presence of a foreign body and with no apparent corneal lesion.

Most cases have occurred in women who have been exposed to alcohol vapor while washing their hair.

The condition is amenable to ordinary treatment and epithelization of the cornea occurs in two, three or four days.

II F CARRASQUILLO

TWO CASES OF PREEPITHELIOMATOUS DYSKERATOSIS OF THE CORNEA
and CONJUNCTIVA (BOWEN'S DISEASE) A PAULO FRIHO and
S R SILVA, Rev brasil de cir 14: 213 (April) 1945

The characteristic signs of Bowen's disease are slightly protuberant and vascularized intraepithelial nodules on the cornea, which have a tendency to spread over the surface and are fragile and irregularly shaped. The microscopic aspect is characterized by disorganized texture. The cells are of various sizes, the protoplasm is normal or slightly granular, the nuclei present variations in form and size and abnormal mitosis. In the superficial layer, round cells of dyskeratosis sometimes surrounded by a membrane, are visible, and histiocytes, lymphocytes and plasma cells are noted in the dermis. Cancerization is always possible. Two cases of Bowen's type of dyskeratosis occurring in men aged 62 and 65, respectively, are presented. Treatment was surgical, and in 1 case there was a recurrence. The treatment indicated is surgical excision, although sometimes total removal of the neoplasm is impossible. In cases of the advanced stage enucleation with removal of the entire bulbar conjunctiva and fornix is indicated. Radium therapy and cauterization are contraindicated.

M E ALVARO

CATARACT DUE TO LOW BLOOD CALCIUM AND ITS MEDICAL TREATMENT
R WEEKERS, Ophthalmologica 107: 257 (May-June) 1944

The author reviews experimental and clinical facts related to the development of cataract associated with low blood calcium. Nine cases are then reported, 7 of which followed thyroidectomy, evidently with inclusion of the parathyroid glands. Two cases followed idiopathic tetany. He believes that in cases following parathyroidectomy cataract

may be prevented by the administration of vitamin D or a preparation known as dihydrotachysterol, together with calcium salts. Early lenticular changes may even be made to regress by this means. F. H. ADLER

Experimental Pathology

CULTIVATION OF HUMAN TUMOR IN THE ANTERIOR CHAMBER OF THE GUINEA-PIG'S EYE. E. M. BLAKE, *Am J Ophth* 29:1098 (Sept) 1946

Blake remarks the success of transplants in the anterior chamber over other regions of the body. He describes a case in which fibrosarcoma of the breast was transplanted to the anterior chamber of a guinea pig and calls attention to the possibilities of utilizing the anterior chamber for research problems. W. S. REESE

ACTION OF NICOTINIC ACID ON THE OPTIC NERVE OF A RABBIT PREVIOUSLY POISONED WITH QUININE MONOCHLOROHYDRATE. E. MARCONCINI, *Arch oftal* 50:19, 1946

Experiments were conducted to determine the effect of nicotinamide on the optic nerve of a rabbit previously treated with quinine monochlorohydrate.

In the rabbit receiving the quinine monochlorohydrate severe degeneration of the myelin sheath of the optic nerve was noted histologically. In the rabbit treated with nicotinamide (P-P factor) the degenerative changes were insignificant. G. B. BIETTI

General

OCULAR DECOMPENSATION. E. M. G. GALTON, *Brit J Ophth* 30:232 (April) 1946

In the armed forces large numbers of persons of both sexes were seen who in the ordinary course of events would never have presented themselves for ophthalmic examination. These persons fell into two groups: men and women whose visual acuity was found during routine testing to fall below required service standards, and those with headache as the main symptom. It was only in the minority that an ocular cause for the headache could be substantiated. It was obvious that the majority had been able to do their civilian work quite happily and without difficulty in the presence of refractive errors of all grades, often with some degree of heterophoria as well. It was only when called on to do other types of work, or the same work under less favorable conditions, that some of them experienced symptoms. In other words, ocular symptoms are due not so much to the defects in themselves as to a breakdown in the compensatory factors which exist in even the so-called normal eye. These factors are complex and involve psychologic and mental as well as physical components. In order to emphasize as strongly as possible the dynamic nature of visual symptoms, it is suggested that the terminology of the cardiologist be adopted. The great advantage of the term decompensation is that it implies the possibility of compensation. To

say that a patient has a decompensated exophoria of 12 degrees implies that not only is he having symptoms from his defect but that with treatment his previous state of compensation can be attained. If a patient with low hypermetropia suddenly complains of trouble after near work, he has decompensated hypermetropia and can in the majority of cases be treated without glasses.

W ZENTMAYER

General Diseases

REPORT OF A CASE OF IRIDOCYCLITIS ASSOCIATED WITH CHICKENPOX
J W HALLETT, *Am J Ophth* 29: 459 (April) 1946

Hallett reports a case of iridocyclitis in a 7 year old boy three days after he contracted chickenpox. Although the attack was severe, the eye recovered fully.

W S RERSE

EPIDEMIC KERATO-CONJUNCTIVITIS ASSOCIATED WITH SKIN LESIONS
W J O'DONOVAN and I C MICHAELSON, *Brit J Ophth* 30: 193 (April) 1946

The cases reported occurred in a general hospital in Egypt during the year 1944-1945.

In 33 of the 66 cases of keratoconjunctivitis there was a concurrent disease of the skin. In 18 of the 33 cases a seborrheic dermatitis was present. In all cases the scalp or face was affected. There was a strong tendency for the cutaneous and ocular lesions to be ipsilateral. In the majority of the cases the onset of the cutaneous lesion preceded that of the ocular one by a definite, but short, interval. A comparison of 33 cases of epidemic virus keratoconjunctivitis without lesions of the skin and the 18 cases with such lesions suggests that the keratoconjunctivitis in the cases with cutaneous lesions was clinically indistinguishable from epidemic virus keratoconjunctivitis.

Lesions of the skin of the face or scalp, especially those of a seborrheic nature, are associated in some cases with keratoconjunctivitis which, on clinical grounds, appears identical with that described as epidemic virus keratoconjunctivitis. The possible analogous nature of the cutaneous lesions of herpes simplex and herpes zoster and in certain cases of epidemic keratoconjunctivitis has been suggested, though by no means proved.

W ZENTMAYER

THE RELATION OF CORNEAL VASCULARISATION AND CONJUNCTIVAL TRANSPARENCY TO GENERAL DISEASE P A GARDINER, *Brit J Ophth* 30: 225 (April) 1946

This study is based on the examination of 190 unselected members of an R A F hospital staff. A second group was examined which consisted of 150 service personnel who were ill. The diseases were all of a chronic nature. The results obtained from this investigation indicate that examination of the conjunctiva and cornea with a slit lamp provides a clue to the amount of trivial sickness in a group of people over a period varying from three months to two years before examination and also to the amount of sickness they are likely to have in the three months after examination. It is possible to say that persons with a high degree of

corneal vascularity are as a group more likely to report sick than those with a low degree of vascularity. The observations on the conjunctiva must be considered with more reserve, but persons with a high transparency reported sick nearly twice as often before examination as those with a low transparency. The degree of conjunctival transparency and the degree of superficial vascularization of the cornea are shown to be higher in chronically ill persons than in healthy persons. The degree of superficial vascularization of the cornea and the degree of transparency of the conjunctiva are shown to have a relation to the incidence of sickness in a group of healthy people.

W ZENTMAYER

OCULAR CHANGES IN A CASE OF RIBOFLAVIN DEFICIENCY G BASSI
and S JONA, *Boll d'ocul* 24: 3, 1945

A 12 year old boy presented the following ocular changes (1) superficial corneal vascularization, (2) pericorneal injection, (3) clouded aqueous and (4) lacrimation and photophobia. After the daily administration of riboflavin the ocular lesions disappeared completely, only to recur when treatment was discontinued.

G B BIETTI

THE RETICULOENDOTHELIAL SYSTEM IN OPHTHALMOLOGY V ROSSI,
Arch oftal 50: 1, 1946

The author calls attention to the abundance of reticuloendothelial tissue in the eye, with special reference to its presence in the uveal tract. He briefly reviews the ocular manifestations associated with disorders of reticuloendothelial tissue, the most typical of which are those seen with chronic articular rheumatism, Heerfordt's syndrome (subchronic uveoparotid fever), Niemann-Pick disease and Schuller-Christian disease.

He describes a case of mycosis fungoides (malignant reticular metaplasia) with choriorretinal changes. The patient, a man aged 55, presented a papuloerythematous eruption of the skin of the lid, conjunctival chemosis and tumefaction of the preauricular node, with papilledema, retinal edema, retinal hemorrhages and dilated and tortuous retinal veins.

G B BIETTI

Hygiene, Sociology, Education and History

THE OPHTHALMOLOGIST AND THE LAWS CONCERNING MILITARY PENSIONS JEAN VOISIN, *Arch d'opht* 5:332, 1945

This article is a review of the French laws in regard to military pensions and indemnities. The laws which have been passed in France from 1887 up to the present are reviewed. The author points out the importance of the ophthalmologist in the handling of cases involving pensions and in consultation in regard to their authorization.

S B MARLOW

Injuries

AN OPERATION FOR POSTERIOR ROUTE EXTRACTION OF INTRAOCULAR FOREIGN BODIES L B SOMERVILLE-LARGE, *Brit J Ophth* 30: 208 (April) 1946

The operation is described in detail. The essential features are summarized as follows. An ample conjunctival flap is cut from before

backward and the episclera completely removed from the trephine site. The sclera over the area that is estimated as nearest the foreign body is trephined with a 1.5 mm trephine. The base of the disk is dissected from the choroid. The choroid is then coagulated through the trephine hole, with the sharp point of the diathermy apparatus. The tip of the 1.5 mm point of the magnet is made to enter the hole. The following advantages are claimed for the trephine operation: (1) apposition of a powerful magnet point as near the foreign body as is compatible with safety, (2) production of a minimum choroidal scar, (3) absence of postoperative hemorrhages in the fundus and opacities in the vitreous.

W. ZENTMAYER

INTRAOCCULAR FOREIGN BODY TOLERATED FOR ELEVEN YEARS
B. DA LUZ and R. SIBAS, *Rev. bras. oftal.* 4: 33 (June) 1946

Eleven years previously the patient received a penetrating wound from a fragment of steel. A roentgenogram showed a foreign body, which supposedly was removed. For a period of six months preceding this report the eye had been painful. The sequelae of endocyclitis with iridodonesis and evidence of a peripheral iridectomy were present. The eye was enucleated, and a fragment of oxidized iron was found embedded in the sclera 3 mm behind the equator of the globe.

M. E. ALVARO

Lens

ATOPIC CATARACTS. F. C. CORDIS and R. CORDIRO-MORFNO, *Am. J. Ophth.* 29: 402 (April) 1946

Four cases of cataract in patients with atopic dermatitis are reported. A brief resume of the theory of allergy is given, in particular, that of Coca, who coined the word "atopy" because it would seem that cataract formation must be considered an uncommon part of the syndrome. The authors feel that the theory of the atopic shock organ is admissible.

W. S. REESE

THE RELATIONSHIP OF RUBELLA IN THE MOTHER TO CONGENITAL CATARACTS IN THE CHILD. E. L. GOAR and C. R. POTTS, *Am. J. Ophth.* 29: 566 (May) 1946

Goar and Potts report 7 cases of congenital cataract, in all but 1 of which the mother had had rubella. Fair results in all were obtained by the Ziegler through and through dissection.

W. S. REESE

ULTRARAPID OPACIFICATION AND SPONTANEOUS ABSORPTION OF THE CRYSTALLINE LENS. C. ESPILDORA-LUQUE, G. O'REILLY and E. MANNS, *Arch. chilena de oftal.* 1: 12 (July-Aug.) 1944

A young man aged 23, who had previously lost the left eye in an accident, had rapid opacification and subsequent absorption of the lens of the right eye. The patient was myopic. He had had a stationary small posterior cortical cataract. Without any apparent cause, the lens became completely opaque in forty-eight hours. This was accompanied with severe pain and congestion of the anterior segment of the eye, but no signs of hypertension or inflammatory reaction were evident. Roent-

genograms of the teeth showed a premolar with a metal filling extending all the way to the apex. This tooth was extracted, and dramatic disappearance of the symptoms and absorption of the cataractous lens took place. The eye returned to normal, and vision was normal with a correction of + 3.50 D.

The authors express the belief that the cataract was brought about by a toxic chemical action from the metal in the filling of the bicuspid.

H. F. CARRASQUILLO

Neurology

DYSTROPHIA MYOTONICA (STEINERT'S DISEASE) IMPORTANCE OF CATARACT AND DISTURBANCES OF METABOLISM THERAPEUTIC EFFECTS OF VITAMIN E. A. FRANCESCHETTI and R. S. MACH, *Helvet med acta* 11:887, 1944

Franceschetti and Mach describe 3 personally observed cases of dystrophia myotonica and stress the importance of cataract in the differential diagnosis. In the atypical forms of Steinert's disease only the presence of a cataract permits a definite diagnosis. The biomicroscopic examination of the crystalline lens is indispensable for the differentiation of myotonic dystrophy from other myopathies, particularly from congenital myotonia. The appearance of creatinuria after an amino-acetic acid tolerance test is of great diagnostic value in that in cases of progressive muscular atrophy, congenital myotonia, myasthenia gravis and the muscular atrophies of the Charcot-Marie type creatinuria is nearly always increased after the test, but neither spontaneous nor induced creatinuria is necessarily present in cases of myotonic dystrophy. They observed the favorable effect of vitamin E in a case of myotonic dystrophy, as well as in a case of idiopathic (pseudohypertrophic) muscular dystrophy (Erb's disease). The therapeutic effect of vitamin E on the muscular function is accompanied with improvement in the creatine metabolism. Myotonic dystrophy has a special place in that some of its symptoms indicate a lesion of the endocrine glands, whereas others indicate a nervous origin. It is possible that both these factors are involved.

J. A. M. A. (W. ZENTMAYER)

Operations

THROMBIN TECHNIQUE IN OPHTHALMIC SURGERY. T. G. W. PARRY and G. C. LASZLO, *Brit J Ophth* 30:176 (March) 1946

Plastic surgeons apply thrombin to the actual surfaces of the graft and bed, and it is generally agreed that the adhesion of such a graft becomes firm enough in many cases to dispense with sutures. It was thought that thrombin might be of greatest value, if successful, in cataract surgery and in conjunctival plastic procedures involving the conjunctiva in general, as in cases of squint.

In cataract operations the section was made in the usual manner with a large conjunctival flap. After completing the removal of the lens, the flap was grasped in two forceps and turned with its inner surface upward. Previously prepared thrombin was instilled on to the turned-up surface and on to the raw area of the globe and the flap placed back and ironed out—in some cases the thrombin was introduced under the flap while in place.

In cases of squint, surgical gut was used for suturing the muscle and thrombin instilled over the whole area of operation, then the edges of the conjunctival wound were immediately brought into apposition and held in this position for approximately one minute.

In a few cases slight crushing together of the edges of the wound with a toothed fixation forceps was carried out.

The hemostatic power of thrombin was also noticeable and this property alone might well be made further use of in ophthalmic surgery.

W ZENTMAYER

Orbit, Eyeball and Accessory Sinuses

BEHAVIOR OF INTRAOCULAR TENSION FOLLOWING SURGICAL PROCEDURES ON THE ABDOMEN G MISSIROLI, *Boll d'ocul* 24: 137, 1945

In 1940 Bietti demonstrated the occurrence of a marked fall in intraocular tension following intestinal occlusion. Boletti later confirmed these observations experimentally. Missiroli states that ocular hypotony also occurs after various abdominal operations, especially gastric resection, and after intestinal perforation and concludes that there is a definite relationship between the patient's postoperative course and the behavior of the intraocular tension. He believes that this sign has a definite prognostic value in evaluating the course of the surgical condition.

G B BIETTI

Parasites

SCHISTOSOMIASIS OF THE CONJUNCTIVA G BADIR, *Brit J Ophth* 30: 215 (April) 1946

Schistosomiasis of the conjunctiva is rare in relation to the large number of patients with schistosomiasis in Egypt. This relative rarity may be either because schistosome infection through the conjunctiva is exceptional or because infection of the conjunctiva with this worm passes unnoticed by the patient until cured with the urinary infection through specific treatment. A case of schistosomiasis occurring in a boy aged 12 years is reported. A tumor had been present in the palpebral conjunctiva of the left upper eyelid near the inner canthus for more than a month. Both eyes showed cicatrizing trachoma with pseudocysts (T3). The swelling was excised. A provisional diagnosis of hypertrophied tarsus was made. The pathologic examination showed a large number of terminal-spined schistosome ova arranged in groups and surrounded by tuberculoid nodules of various sizes. A male and a female schistosome were seen in cross section, lying in a dilated branch of the superior orbital vein. The pathologic report is given in detail. There is a discussion of the way in which the schistosomes reach the conjunctiva and of the possibility that the adult worms may pass from the portal to the systemic circulation through the large anastomotic veins between the two systems.

The article is illustrated.

W ZENTMAYER

The Pupil

CLINICAL ASPECTS OF THE PROBLEM OF THE TONIC PUPIL MARIA ANDREA-VAN LEEUWEN, *Ophthalmologica* 111: 339 (June) 1946

This paper deals chiefly with the question of whether the tonic pupil has a hereditary basis. It was not possible to obtain any evidence

of this, and neither the patients with tonic pupil nor their relatives show any signs of a congenital degenerative disorder of the central nervous system. The families examined, however, showed a definite hereditary basis of allergic and angioneurotic manifestations. Herpes zoster was noted to have occurred frequently among the patients with tonic pupil and their relatives. This peculiar fact, according to the author, justifies a systematic search in further cases of tonic pupil and amongst the patients' families.

F H ADLER

Retina and Optic Nerve

RECURRENT EDEMA OF THE MACULA, OR SEROUS CENTRAL RETINITIS
D DIAZ DOMINGUEZ and E ARQUES GIRONA, Arch Soc de oftal hispano-am 6:38 (Jan) 1946

The authors describe a condition of the retina under the name recurrent edema of the macula, or serous central retinitis. They believe that the condition is similar to that described by other observers on different occasions (von Graefe, in 1860, and, later, Guist, Gissy, Fritz Rank, Horniker, Asayansa and others) under various names, such as central recurrent retinitis, periretinal edema, ablatio retinal macularis, capillary spastic retinitis and serous central retinitis.

The condition when reported by von Graefe was supposedly rare, but according to the authors it is seen comparatively frequently. They have observed 14 cases.

The patients complain of a veil in front of the eyes which annoys them, their visual acuity, however, is normal. Ophthalmoscopic study reveals a bright raised circular area in the macula containing disseminated white or yellowish white dots. The condition occurs in adults, is not serious and disappears after a time without any definite treatment. It has, however, a tendency to recur. The etiology of the disease is unknown.

H F CARRASQUILLO

Therapeutics

THE THERAPEUTIC TREATMENT OF UVEITIS ASSOCIATED WITH TOXOPLASMOSIS
A C KRAUSE and L F SMITH, Am J Ophth 29: 977 (Aug) 1946

Krause and Smith conclude that the sulfonamide compounds with typhoid therapy may have value in the treatment of uveitis associated with toxoplasmosis.

W S REESE

THE USE OF CRYSTALLINE PENICILLIN IN CORNEAL AND INTRAOCULAR INFECTION
F JULER and G T JOHNSON, Brit J Ophth 30:204 (April) 1946

The authors have found the use of crystalline penicillin to have been beneficial in treatment of infective ulceration of the cornea, deep recurrences of keratitis rosacea, infections through the filtration scar of a trephine operation, infections of perforating wounds and in intraocular operations. Sodium penicillinate was used, it is emphasized that the

drug be rubbed well under any advancing edge of ulceration and into any infiltration. No evidence of harm to the tissues has been seen.

W ZENTMAYER

OCCUPATIONAL THERAPY IN EYE WARDS W O G TAYLOR, Brit J Ophth 30.456 (Aug) 1946

Taylor enumerates the following crafts suitable for patients with ocular disorders who need occupational therapy, roughly graded in terms of the amount of vision required, although all can actually be performed by the blind: rug wool weaving, Persian rug knotting, macramé knotting, knitting machine work, basketry, sea grass weaving, weaving on a scarf loom and tablet weaving. The various crafts are illustrated.

W ZENTMAYER

Society Transactions

EDITED BY DR W L BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Brittain F Payne, M D , *Chairman*

Milton L Berliner, M D , *Secretary*

Dec 16, 1946

INSTRUCTION HOUR

Application of Color Vision in Clinical Practice. DR GERALD FONDA,
Newark, N J (by invitation)

A film strip in color, developed at the School of Aviation Medicine, Randolph Field, Texas, was used by courtesy of the School of Aviation Medicine

The film strip demonstrated the appearance of colored lights and the spectrum to the totally color-blind subject and to the subject with red-green blindness, the attributes of color, classification of color vision deficiencies, methods of administering tests with the pseudoisochromatic plates and use of the School of Aviation Medicine's Color Threshold Tester

The use of pseudoisochromatic plates was emphasized as a good screening test and that of the Color Threshold Tester as a quantitative color vision test

There is no cure for congenital color vision deficiencies. An explanation was given of the increase in number of pseudoisochromatic plates read after the so-called cure for color blindness. Reasons were also stated that the Holmgren yarn test is not a good test for color vision

OBITUARIES

Obituary: Robert K Lambert, M D. DR SAMUEL GARTNER

This obituary was published in the February issue of the ARCHIVES, page 232

REPORT OF CASES

**Traumatic Prolapse of the Vitreous into the Anterior Chamber:
Report of a Case Studied with Fluorescein** DR GERALD J
HALTON

Intraocular tension became elevated after trauma to the eye. When the tension would no longer respond to miotics, paracentesis was performed, yielding vitreous, the presence of which in the anterior chamber had not previously been suspected

As a means of studying the extent of prolapse of the vitreous fluorescein was given by mouth, and the prolapsed vitreous showed the fluorescein stain in fifteen minutes. Fluorescein was not noted

in the aqueous surrounding the prolapsed vitreous, nor was it observed in the aqueous of the normal eye

DISCUSSION

DR WILLIS S. KNIGHTON First, this case demonstrated how difficult it is to recognize prolapsed vitreous in the anterior chamber with the slit lamp, especially when its presence is not suspected. Second, it showed how much easier it is to see vitreous after disruption by injury, in this case, paracentesis. Third, it demonstrated the value of fluorescein in determining the extent of vitreous in the anterior chamber.

Treatment of Epiphora by Electrocoagulation DR DAVID J. MORGENSTERN, Brooklyn (by invitation)

Electrocoagulation is valuable in the treatment of epiphora. Applied to the lacrimal and accessory lacrimal glands, it reduces secretion of tears. Lightly applied at the base of an everted punctum, it produces a cicatrix which draws the punctum backward. Spots of electrocoagulation placed more deeply along a relaxed lower lid tighten the lid, making a firm contact with the eyeball. Conjunctival hypertrophy or tumor causing epiphora can be destroyed. In the intranasal operation for drainage of an infected lacrimal sac, the sac is first entered and partially sterilized by means of an insulated electrode passed through the canaliculus. Similarly applied, electrocoagulation combats threatened closure of the new intranasal opening and reopens such a closure occurring after operative drainage of the sac, as well as corrects obstruction anywhere in the lacrimal sac or along the nasolacrimal duct. Such an obstruction may be a polyp, cyst, scar tissue or bony sclerosis. Blockage at the orifice of the duct may similarly be destroyed. The current used is about 1,000 milliamperes when the active electrode is directly connected with the indifferent electrode. In cases of congenital blockage at the lower end of the nasolacrimal duct channelization can be produced. When excessive folds of mucous membrane are present in the duct and abnormal meatal continuation of the duct downward (often terminating in a minute opening or slit) causes tearing, an adequate opening can be formed by electrocoagulation.

PAPER OF THE EVENING

Tobacco Amblyopia DR CHARLES L. SCHIEPENS, Brussels, Belgium

In peacetime there is an unexplained geographic variation in the incidence of tobacco amblyopia.

During the last war it was much more frequent than usual in Belgium. Reasons given are (1) consumption of wartime tobacco, (2) mental shock, and (3) undernourishment, especially the lack of fats and animal proteins. With the diet poor in these substances, the disease appears in younger patients and causes chronic symptoms of general tobacco poisoning. The intake of large doses of vitamin A, thiamine chloride and riboflavin has not affected the course of the disease in my Belgian patients, who had no signs of vitamin B deficiency. These observations can be reconciled with Dr. Carroll's

views by admitting that vitamin B deficiency, when present, is an important etiologic factor in tobacco amblyopia. When it is not present, however, as in my cases, the intake of vitamin B has no effect on the amblyopia.

Careful study of the blood and of hepatic function in malnutritional as well as in tobacco amblyopia may prove useful.

The defects in the visual fields suggest that the disease begins in the retina and not in the optic nerve. The first campimetric sign is enlargement of the normal angioscotoma. Later, the pericecal maze, or lacunar scotoma, contains nuclei (small areas of absolute scotoma). The cecocentral localization of the tobacco scotoma probably results from the greater sensitivity of the macular cones together with a tendency of the normal angioscotoma to enlarge. The cecocentral area is the only place where these two factors overlap. The probable relation of the cecocentral scotoma to a cilioretinal angioscotoma in many instances is stressed.

At a very early stage the field defects of heredofamilial atrophy of the optic nerve and tobacco amblyopia are similar. They consist in pericecal lacunar scotoma, particularly in the cecocentral region. At a later stage, that of Leber's disease, a pericentral scotoma develops, which is related to the lacunar scotoma. Later still, the blindspot itself enlarges, through atrophy of the optic nerve. The character of these field defects may suggest that heredofamilial optic nerve atrophy begins in the optic nerve and not in the retina.

DISCUSSION

DR FRANK D. CARROLL. Considering the conditions that prevailed in Belgium from 1939 to 1942, it is remarkable that Dr Schepens was able to carry on a scientific investigation of the kind he has described. I am glad that we agree on many points. It is rare to see patients with tobacco amblyopia who do not consume at least some alcohol, there is no doubt, however, that there is such a thing as tobacco amblyopia alone. In the literature several hundred cases have been reported. Usher, in a series of 1,100 cases, stated that in over 100 cases the patients were teetotalers. I have seen a small number of patients who did not drink. But in this country most patients with this syndrome do consume alcoholic liquors, sometimes in large amounts. This syndrome can occur in heavy drinkers who do not smoke, but it is rare to find any heavy drinker who does not smoke at least a few cigarettes a day.

I agree with Dr Schepens on the importance of the scotoma rather than of the visual acuity, and his "nasal reading" test is interesting. Patients develop amblyopia during a period of undernourishment or chronic starvation, as Dr Schepens said. One would not think that in this country, where there is plenty of food, one would see persons with chronic starvation. Certainly, most of the patients with amblyopia do not look malnourished. Alcoholic persons frequently do have evidence of vitamin deficiency, but, as I have stated before, none of my patients with tobacco amblyopia have shown any clinical evidence of vitamin deficiency. The only reason that I was encouraged to

treat them with vitamins was that vitamin therapy seemed to do so much good to patients with alcohol amblyopia, or what might better be called nutritional retrobulbar neuritis

Dr Schepens spoke of an ocular disease which was found in persons held as prisoners of war by the Japanese. He pointed out that pericentral scotoma of the type associated with this condition, having a connection with the blindspot, would be rare in persons with tobacco amblyopia. Frequently the vision of these prisoners was 20/70 or 20/100, and in most of them I saw (and I did not see a great many) it did not improve. I do not think that one knows the whole story about this form of amblyopia. One of the patients told the Army physicians that at his camp in the Philippines, where many of the prisoners acquired this condition, they were able to steal some unpolished rice from the Japanese and that over a period of a month or two, while they had this diet of unpolished rice, their vision improved tremendously. When they had to go back to their diet of polished rice, their vision became worse. The only difference between polished and unpolished rice I know of is the thiamine content.

I should like to ask Dr Schepens what tests should be made to determine "hepatic deficiency." Hepatic function tests are not as satisfactory as one would like.

I agree that this condition has a very fluctuating course and that some patients who are expected to recover rapidly do not do so. A very few patients who stopped the use of alcohol and tobacco and who were given a good diet have not shown improvement in vision. I am sure there are some problems and factors which are not yet understood.

DR C. L. SCHLEPENS, Brussels, Belgium. In a case of tobacco amblyopia a number of things are to be borne in mind. The first is that tobacco amblyopia is due to tobacco poisoning, and therefore tobacco still remains the most important factor. The second point is that of diet. It appears to me that several dietary factors have to be considered. In my cases the lack of proteins and the caloric deficiency certainly were the main elements. Since there was no vitamin B deficiency, it is surprising that vitamin therapy was ineffective. In Dr Carroll's cases, on the contrary, there was no caloric deficiency but a vitamin B deficiency existed, as it often does in alcoholic patients. This explains his good results with vitamin therapy. I am under the impression that three dietary factors have an influence on the incidence of tobacco amblyopia: the caloric intake, the animal protein intake and the vitamin B intake.

The third point to be considered in a case of tobacco amblyopia is the possible presence of anemia. An experienced clinician in England told me that in his experience chronic anemia is an etiologic factor in tobacco amblyopia. The fourth point is that of hepatic insufficiency. This is of course a great problem. I am not suggesting that it is wrong not to make any of the various tests for hepatic dysfunction in a case of tobacco amblyopia, but I do not know what test should be made. It is my suggestion that research be carried out on this subject. De Schweinitz observed urobilinuria, and more recently Lundberg noted hyperglycemia, in cases of tobacco amblyopia.

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Burton Chance, M D , Chairman

George F J Kelly, M D , Clerk

Dec 19, 1946

Experimental Investigation of the Pathogenicity of Diphtheroids Isolated from the Human Conjunctiva. DR CHARLES WEISS and MR M C SHEVKY, San Francisco

Diphtheroids resembling *Corynebacterium xerosis* and isolated from the human conjunctiva grow well in a menstruum of mucin. When suspended in this medium and inoculated into the anterior chamber of the eyes of albino rabbits, cultures retain their viability for several days, while in saline solution they are rapidly destroyed.

Intraocular injections into rabbits of cultures of diphtheroids suspended in saline solution produce moderate inflammation of the ciliary process. With suspensions in mucin the reaction lasts longer, is much severer and is associated with acute keratitis. The lesions usually regress spontaneously within two or three weeks.

Killed cultures of diphtheroids in saline solution produce mild inflammatory changes in the ciliary process which are seen in histologic sections, none of the lesions are visible grossly. In a menstruum of mucin the inflammatory reaction is severer. Since mucin alone is relatively innocuous, it is suggested, on the basis of these studies and those of others, that it protects bacteria from the digestive action of humoral and cellular proteolytic enzymes and other immunologic defense mechanisms. Living diphtheroids are thus permitted to grow and exert their pathogenic activity.

By means of the recently developed methods of Muller and Miller and Pappenheimer and Johnson, it was possible to demonstrate that when diphtheroids are grown in a medium of very low iron concentration they yield a toxic filtrate which is injurious to the uvea and cornea, but not to the skin or conjunctiva, of albino rabbits.

Studies which had been planned on the specific chemotherapy and serum therapy of diphtheroids were interrupted because of the war emergency.

On the basis of these investigations, it may be concluded that diphtheroids which are present on the normal or the inflamed conjunctiva may be considered as potential pathogens, which can exert serious injury when they find their way into the interior of the eye.

DISCUSSION

DR LUTHER KAUFFMAN: I wonder whether in treating conditions involving the conjunctiva the proper procedure would be to get rid of the mucin. I am reminded of the treatment of vernal conjunctivitis with a solution of monohydrated sodium carbonate which Dr Lehrfeld presented before this section several years ago.

Does Dr Weiss know whether other bacteria receive the same protection from mucin that these diphtheroids do?

DR BURTON CHANCE: The early death of diphtheroids reminds me of my own experience in the early days of my medical practice when "diphtheria" was an extremely frequent disease. For two winters

I did volunteer work at the old Municipal Hospital, one week 275 sick persons were inspected. Many patients were there because the bacteriologist, who was among the first in the field at that time, had found what he believed to be the diphtheritic organism in material from the conjunctiva and fauces. A few days after the children were admitted, another examination was made, with negative results, this created more than a "headache," both outside and inside the hospital. The children were interested to know whether or not the diagnosis had been correct. The people outside were complaining because their children had been taken away from home and isolated. Having to have their own tooth-brushes and carry out other disinfecting measures were the sources of complaints from the children. There were no signs of the old diphtheria of the conjunctival tissues that had prevailed in earlier times. My teachers would refuse to accept a diagnosis of diphtheria unless there were actual structural and infiltrative changes. Dr. Weiss's statement concerning the evanescence of the diphtheroids, therefore, reminded me of that somewhat confusing experience.

DR CHARLES WEISS, San Francisco. In answer to Dr. Kauffman's question. In general, mucin on the inflamed conjunctiva is due to bacteria. Of course, it may also be due to chemical irritants. On the basis of our work, it seems reasonable to remove it. I mentioned in the course of my presentation that the virulence of a number of other bacteria is increased by mucin. Among them are the meningococcus, the gonococcus, *Vibrio comma* (cholerae) and the virus of influenza.

Experiences in Testing Color Vision of Persons with Defective Color Sense DR BURTON CHANCE

Dr. Chance stated that early in life he became aware that some persons were color blind, and ever since he had been interested in color. In recent years defective color vision has become the subject of so much investigation that he ventured to tell something of his own interest in it, and to express his beliefs.

The perception of color by human beings is an intellectual process involving psychologic and physiologic factors operating with the effects of light on the chemical elements in the retina. The average person is able to distinguish all seven colors in the visible spectrum—it is not improbable that animals and birds perceive beyond what mankind can define. There occasionally is found a person whose appreciable "spectrum" is shortened at one end or at both ends and others to whom the ends of the spectrum are only somewhat indistinct—hence the appellation color blind. A better and kinder name is "achromatopsia." More men than women are affected. The defect is transmitted from one generation to another through females who may not themselves be known to be affected. In pure cases of color blindness the structures of the eyes are not visibly changed. Disease of the retinobulbar may be accompanied with defective color perception, however, the defect in color vision is usually not comparable to that of the persons with a congenital deficiency. A singular anomaly is that presented by several persons with a unilateral deficiency.

The measurement of color perception has aroused serious consideration in the arts and has presented important problems in transportation,

as well as in the selection of members of the military forces. Many persons notable in history have had deficient color perception. Since this defect was pronounced in John Dalton, the famous English physicist, he gave it deep study and devised various schemes for its testing.

Color vision tests have utilized dyed wools, colored charts and colored lights which are compared or matched with certain standard colors, selected after prolonged investigation. In practice, red and green have been the colors for which vision has most frequently been found to be deficient, hence those colors have been adopted as the basic standard for all tests.

Color perception is an unsolved mystery. Many theories have been proposed, but none solves all the problems—their respective advocates are violent contenders for their hypotheses. Thus far, the theory offered by Thomas Young, and later arrived at by similar means by von Helmholtz, has the least uncertainty. According to their theory, each color excites its own system of retinal fibers to the brain.

Being a congenital defect, color blindness cannot be cured, or even reduced—all schemes proposed are only false promises. Subjects can be trained to distinguish one color from another more fully than was possible before intensive training was begun, yet when standard lights or plates are modified, as by foggy atmosphere or color dilutions, the natural defects become manifest.

All subjects have not identical defects, some lack perception of one or two, others of more, even all seven, colors. Observers, therefore, have classified them according to the number. Some showing only a lessening of the color strength are classed as having anomalous vision for those color classes. Increasing attention to "anomalous" color vision is being carried on today. Persons to whom all colored objects are as though they were black are spoken of as having monochromatic vision. Despite all the interest evinced in the past fifty years, no new fundamental aspects of the problem have been solved, their solution rests with the photochemistry of the retina.

DR GEORGE F J KELLY. Dr Chance spoke of several cases in which there was normal color perception in one eye and abnormal color perception in the fellow eye. Was there any evidence of pathologic change in the fundus of the abnormal eye?

DR P ROBB McDONALD. I have been interested in Dr Chance's paper because for part of the time that I was in the service I was working with persons who were engaged in developing tests of color vision.

I notice that he also used the term "defective color vision." This is a much more appropriate term than "color blindness." There are many people who have defective color vision but who are by no means color blind. In setting up tests for color vision there were certain requirements. They were essentially as follows: (1) a "job analysis" to determine what color discriminations were actually required, e g, of pilots, bombardiers and air crew, (2) evaluation of the tests of color vision that were available, (3) development of new tests, (4) determination of the reproducibility, reliability and validity of the tests that were adopted.

The problem of landing a plane in the daytime was not too difficult because clues other than color were usually employed to determine whether one was about to land on a tilted or on a flat surface. At night the problem was more difficult. The runway markers might be colored lights of low intensity, the landing might be made with glide path indicators, or the only communication between the tower and the pilot might be made by a directional light, such as the "biscuit gun." Men who worked about the airplane also had to make certain color discriminations, for example, the wiring was usually coded by color, and the various fuses had color codes.

What every one wanted was a quantitative test of color vision. One of the closest approaches to this was a lantern developed by Dr. Louise Sloan Rowland. The test was modified from one developed by the Royal Canadian Air Force, which, in turn, was a modification of the Williams lantern. The test was called a color threshold test and consisted in presenting eight different colored lights at eight different intensities of illumination. The minimum intensity was that at which most normal persons called the color correctly. A score of 62 to 64 was considered normal.

We were fortunate in having a considerable number of persons with defective color vision at Randolph Field, and Dr. Sloan was able to test them with various tests of color vision. In all, about six tests were used—the Ishihara, the American Optical Company's pseudo-isochromatic plates, an abridged edition of the same, the Rabkin polychromatic plates, an anomaloscope test and the Color Threshold Tester. Several other tests were employed at one time or another. Either before or after this battery of tests the subjects were given "practical" tests, such as the identification of colored flares actually fired from an airplane, the identification of colored signal lights and the identification of colored codes on wires.

On the basis of the results, the Color Threshold Tester was the closest approximation to a quantitative test. In the future there may be two types of color vision tests: one that can be given in the office to determine whether a subject is normal or not, and one the military may use to determine whether the subject has safe color vision or not.

DR. BURTON CHANCE. In the several instances in which I had seen perfect color vision in one eye and defective color perception on the other there were no visible changes in the fundus. If it is true that the perception of color is generated by the action of light on the retinal pigment, it is more than likely that there was something constitutionally lacking in the color-blind eyes that gave rise to the defect. Therefore, in this consideration, I should not class a case of unilateral color blindness presenting changes in the fundus as a case of true color blindness.

I wish to thank Dr. McDonald for telling us something of what was done in the Army in the last war, I regret that I was afforded no opportunity to witness such studies personally.

Book Reviews

Squint and Convergence: A Study of Di-Ophthalmology. By N A Stutterheim Price, 15s Pp 95, with 26 graphs and 15 diagrams London, England H K Lewis & Co, Ltd, 1946

This book attempts to give a new theory of the origin of comitant strabismus. The work is difficult to evaluate because it lacks clarity of expression. In his previous book, "Indications for the Kinetic Treatment of the Eyes," published in 1931, the author evolved the concept that "not fusion sense but what I called involuntary convergence, the basic movement of the di-ophthalmos or the bi-unial eye, is the kinetic power for bi-foveal single vision."

He starts with the assumption, which is undoubtedly correct, that the cause of comitant squint is to be found in some supranuclear pathway. From this point on, his reasoning is difficult to follow and he comes to the conclusion that "squint is that condition of human vision (the bi-foveal eye) where convergence and its correlate—namely the bi-fovea—are in abeyance."

One gets the impression from reading the book that the ideas it contains have merit but that they could be better expressed.

The second part of the book deals with therapy. This consists in what the author calls kinetic treatment of reflex convergence with a battery of prisms, based on the physiologic law of facilitation of reflexes.

FRANCIS HEED ADLER

Monocular Vision Training By Mildred Smith Evans Price, \$3 Pp 100, with 28 lessons and 18 drawings. Baltimore Williams & Wilkins Company, 1946

The author has arranged a series of graded daily tasks for amblyopic eyes covering a period of approximately one month. These include such stock devices for improving eye-hand coordination as tracing and dot drawing. The text, printed in boldface ranging from 24 to 10 point, embodies directions for the exercises, original stories and questions, provocative of thought as well as visual discrimination.

A space is provided in which to write the time required to complete each lesson. This is a worthwhile detail, for speed must combine with accuracy in meeting the visual tasks of daily life. It was found that a boy of 7 years with a visual acuity of 6/20 (20/70) in his amblyopic eye required approximately one-half hour to finish each daily task. Mrs. Evans has evidently apportioned her material well.

The book is obviously limited, however, in the amount of material it offers. Unfortunately, permanent normal vision can rarely be restored to an amblyopic eye in a month's time. (The inclusion of several tracing sheets instead of one for each picture would contribute toward giving the training a longer time spread.) There is a further limitation in the text, the reading and interpretation of which would be too difficult

for the average child under 7 years of age. Much of the most effective work with amblyopia is accomplished with children under this age.

The price may seem high on first consideration and undoubtedly makes the purchase of this volume prohibitive for most clinic patients. When compared with the cost of half-hour weekly treatments in a private office, \$3.00 is not an excessive outlay for four weeks' daily homework.

Mrs. Evans has made a start in the right direction. More such planned exercises are needed. The American Association of Orthoptic Technicians might well make the assembling of a graded library of amblyopic material one of its major projects.

ELIZABETH K. STARK

The Eye Manifestations of Internal Diseases By I. S. Tassman, M.D. Second edition. Pp. 614, with 243 illustrations, 24 in color. St. Louis: C. V. Mosby Company, 1946.

According to the author, this book is designed to serve the needs of the ophthalmologist and all others engaged in general or specialized practice. I suppose that Dr. Tassman has steered this difficult middle course as well as could be expected, but his work suffers from the numerous compromises that have had to be made. For example, several chapters are devoted to a description of the eye and its adnexa, the examination of the patient and the routine tests and equipment therein employed. I believe that much of this could have been omitted—the ophthalmologist does not need such primary instruction, and the general practitioner is unlikely either to perform the simpler procedures or to buy the equipment necessary to carry out the more elaborate examinations.

The second part of the book, beginning at chapter VI, describes the ocular manifestations of systemic diseases. The systemic disease is first described, and the consequent ocular lesions are then taken up in adequate, if not encyclopedic, detail. The headings include "Structural, Congenital and Hereditary Manifestations", "Infections and Focal Infectious Diseases", "Tuberculosis, Virus, Fungus, and Parasitic Infections", "Drug Intoxications", "Diseases of the Cardiovascular System, Blood, Endocrine Glands, Nervous System, Skin and Bone," and "Disorders of Menstruation, Pregnancy, Metabolism and Nutrition." There is a separate chapter on intracranial tumors.

The illustrations, particularly those in color, are good. Unfortunately, most of the reproductions of fundus photography have not come out well, and future editions would be improved if these photographs could be replaced with drawings.

This book lacks the conciseness of its classic predecessors, notably the works of Knapp and Foster Moore, but its faults are more than balanced by its virtues. I have enjoyed reading it and have already referred to it more than once with profit to myself and my patients. I consider it a useful work and have no hesitation in recommending it.

G. M. BRUCE

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